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AGRICULTURAL PATENT REFORM ACT

M-127
ORIGINAL

HEARING

BEFORE THE

SUBCOMMITTEE ON
PATENTS, COPYRIGHTS AND TRADEMARKS

OF THE

COMMITTEE ON THE JUDICIARY
UNITED STATES SENATE

NINETY-NINTH CONGRESS

FIRST SESSION

ON

S. 1093

A BILL TO AMEND THE PATENT LAW TO RESTORE THE TERM OF THE PATENT GRANT IN THE CASE OF CERTAIN PRODUCTS FOR THE TIME OF THE REGULATORY REVIEW PERIOD PREVENTING THE MARKETING OF THE PRODUCT CLAIMED IN A PATENT

SEPTEMBER 10, 1985

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I

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CONTENTS

STATEMENTS OF COMMITTEE MEMBERS

Page
Mathias, Hon. Charles McC., Jr., a U.S. Senator from the State of Maryland, chairman, Subcommittee on Patents, Copyrights and Trademarks 1
Metzenbaum, Hon. Howard M., a U.S. Senator from the State of Ohio 20

PROPOSED LEGISLATION

S. 1093, a bill to amend the patent law to restore the term of the patent grant in the case of certain products for the time of the regulatory review period preventing the marketing of the product claimed in a patent 3

CHRONOLOGICAL LIST OF WITNESSES

Quigg, Hon. Donald J., Acting Commissioner, Patent and Trademark Office, Washington, DC, accompanied by Charles E. Van Horn, director, Patent Examining Group 120, Organic Chemistry and Biotechnology, and H. Dieter Hoinkes, lawyer, Legislation and International Affairs, U.S. Patent and Trademark Office 22
Cawley, Hon. Wayne A., Jr., secretary of agriculture, Maryland Department of Agriculture, Annapolis, MD; Henry Holloway, president, Maryland Farm Bureau, Randallstown, MD; Jack Early, president, National Agricultural Chemicals Association, Washington, DC, accompanied by Vaughn D. Bryson, president, Elanco Products, division of Eli Lilly Corp., Indianapolis, IN, and Edwin Tocker, senior attorney with E.I. du Pont de Nemours & Co., chairman of NACA's Patent Committee 32
Doyle, Jack, director of Agricultural Resources, Environmental Policy Institute, Washington, DC; and William F. Haddad, president, Generic Pharmaceutical Industry Association, New York, NY 55

ALPHABETICAL LIST AND MATERIAL SUBMITTED

Bryson, Vaughn D.: Testimony 49
Cawley, Wayne A., Jr.:
  Testimony 32
  Prepared statement 33
Doyle, Jack:
  Testimony 55
  Prepared statement 59
  EPI memo to members of the House Judiciary Committee, August 7, 1984 62
    Enclosures:
      Table of market shares for selected pesticides 64
      "Pesticide Bill Change Mystifies Lawmaker," by Ward Sinclair, from the Washington Post, August 1, 1984 65
      "Critics Score Agricultural Drug Bill," from the Congressional Quarterly, August 11, 1984 66
Early, Jack:
  Testimony 34
  Prepared statement of the National Agricultural Chemical Association 36
  Additional comments 41
Haddad, William F.:
  Testimony 67
  Prepared statement 70
Hoinkes, H. Dieter: Testimony 24

Page
Holloway, Henry: Testimony 33
Quigg, Donald J.:
  Testimony 22
  Prepared statement 26

APPENDIX

Statement of the Animal Health Institute 77
Memos to:
  Neville P. Clarke, from Melvin J. DeGeeter, The Texas Agricultural Experiment Station, The Texas A&M University System, May 31, 1985 87
  Michael Lytle, special assistant to the Chancellor for Federal Relations, from the Texas Agricultural Extension Service, The Texas A&M University System, May 31, 1985 89

CORRESPONDENCE

Letter to Hon. Strom Thurmond, chairman, Committee on the Judiciary, from Douglas A. Riggs, general counsel of the U.S. Department of Commerce, September 6, 1985 90
  Enclosure: Detailed Comments on S. 1093, the "Agricultural Patent Reform Act of 1985" 92
Letters to Hon. Charles McC. Mathias, Jr., chairman, Subcommittee on Patents, Copyrights and Trademarks, Committee on the Judiciary, from:
  Richard E. Sanderson, Acting Assistant Administrator for External Affairs, U.S. Environmental Protection Agency, September 9, 1985 95
    Enclosure: Comments of the EPA on S. 1093, "Agricultural Patent Reform Act of 1985" 96
  Jennifer Joy Manson, Assistant Administrator for External Affairs, U.S. Environmental Protection Agency, December 13, 1985 99
    Enclosure: Response to Senator Mathias' letter of November 5, 1985 100
  Varel Bailey, president, National Corn Growers Association, September 23, 1985 101
  Donald W. Banner, president, Intellectual Property Owners, Inc., October 10, 1985 102
  R. Allen Davis, president, Maryland Grain Producers Association, Inc 103
  Charles A. Black, executive chairman of the board, Council for Agricultural Science and Technology, November 13, 1985 104
    Enclosures:
      "Impact of Government Regulations on Development of Chemicals Used in Animal Production," CAST Report No. 85, October 1980 107
        Attachment 1—New Animal Drug Application 124
        Attachment 2—Internal Bureau of Foods Processing of Animal Drug Petitions 128
        Attachment 3—Regulation of Essential Nutrient Additions to Animal Diets, by D. E. Ullrey 133
      "Impact of Government Regulation on the Development of Chemical Pesticides for Agriculture and Forestry," CAST Report No. 87, January 1981 137
      "Plant Germplasm Preservation and Utilization in U.S. Agriculture," excerpt from CAST Report No. 106, November 1985 160
  John Harvey, Jr., chairman, Division of Agrochemicals of the American Chemical Society," November 20, 1985 169
  C. Michael Hoback, Confidential Assistant to the Assistant Secretary for Science and Education, Department of Agriculture, December 9, 1985 170

NEWSPAPER ARTICLES

"Momentum Favoring Ag Chemical Firms' Predicament," from the Delmarva Farmer, August 6, 1985 171
Comment—"The 'Agricultural Patent Reform Act'," from the Delmarva Farmer, August 13, 1985 172

AGRICULTURAL PATENT REFORM ACT

TUESDAY, SEPTEMBER 10, 1985

U.S. SENATE,
COMMITTEE ON THE JUDICIARY,
SUBCOMMITTEE ON PATENTS, COPYRIGHTS AND TRADEMARKS,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:07 a.m., in room SD-226, Dirksen Senate Office Building, Hon. Charles McC. Mathias, Jr. (chairman of the subcommittee), presiding.

Also present: Senators Metzenbaum and Kennedy.

Staff Present: Steven J. Metalitz, Pam Batstone, Charles Borden, and Matt Gerson from the Subcommittee on Patents, Copyrights and Trademarks; Eddie Correia, counsel to Senator Metzenbaum; Beverly McKittrick, counsel to Senator Laxalt; Jodi Brayton, counsel to Senator Simpson; Andrew Hartsfield, counsel to Senator Denton; Arthur Briskman and Peggy Mainor, counsels to Senator Heflin.

OPENING STATEMENT OF HON. CHARLES McC. MATHIAS, JR., A U.S. SENATOR FROM THE STATE OF MARYLAND, CHAIRMAN, SUBCOMMITTEE ON PATENTS, COPYRIGHTS AND TRADEMARKS

Senator **MATHIAS**. The Subcommittee on Patents, Copyrights and Trademarks is meeting today to take testimony on the agricultural patent reform bill, Senate bill 1093, introduced earlier this year.

This is an effort to continue the work that was done last year in the human pharmaceutical area, culminating in the enactment of Public Law 98-417, the Pharmaceutical Patent Term Restoration Act. The second title of that law provides for limited restoration of patent time for human pharmaceutical drugs that unavoidably lose substantial patent life during the Federal safety and efficacy tests that they must clear before being brought to the public. In the same vein, Senate bill 1093 allows an extension of patent life up to 5 years for agricultural chemicals and veterinary medicines for time lost in regulatory review procedures at the Environmental Protection Agency and the Food and Drug Administration. Both of these agencies are planning to submit statements to explain those procedures to the committee.

For about 5 years, I have thought that it would be desirable to provide patent term restoration in those industries which are impacted significantly by the loss of patent life because of the time that is required for premarket regulatory tests. I think we should be clear that no member of this committee, no Member of the Congress, doubts the need for the most stringent and careful kind of testing; that is not what is at issue here. What we are saying is that an adjustment should be made in the patent treatment of these inventions, adding some time at the end of the patent term to compensate for the time lost at the beginning of the patent term. It is a very simple matter of equity. The innovative chemicals for protecting food crops should have the same patent life as other products: one homely example would be a floor wax. And the same principle of equity applies to the other chemical products addressed by Senate bill 1093—the veterinary medicines that preserve the health of farm animals and domestic pets.

It is well documented that agricultural chemicals, such as pesticides, rodenticides, and herbicides, now lose an average of 5 to 7 years of patent life during the EPA approval process. I think it is up to us to ensure that the system of incentives that has worked in the past in this crucial area remains intact to fuel inventive genius in the future. It is true that the prices farmers pay for pesticides and animal drugs can drop when the patent expires. But it is also true that extending the patent term could lower prices for farmers, since manufacturers can recoup their investment in research and development over a longer period. Most importantly, farmers understand the importance of new agrichemical and veterinary breakthroughs that will increase productivity. Accordingly, I am glad to say that Senate bill 1093 enjoys the support of the American Farm Bureau, the National Farmers Organization, and the National Farmers Union. I am pleased that the secretary of agriculture for the State of Maryland, Mr. Cawley, and a spokesman for the Maryland Farm Bureau will also testify.

Finally, I would like to mention the negotiations that are now under way between the agrichemical manufacturing industry and some environmental public interest organizations concerning amendments to the Federal Insecticide, Fungicide and Rodenticide Act. These negotiations are expected to be completed in early October. I believe that in the eyes of some of the public interest groups, acceptance of the patent reform bill is firmly tied to progress on these amendments.

Now, there are two separate issues, and they ought to be considered independently. But I think we all recognize that this is a delicate situation and, therefore, I would suggest that the committee take no further legislative action on S. 1093 until these negotiations have had a chance to run their course.

[S. 1093, introduced by Senator Mathias, follows:]

II

99TH CONGRESS
1ST SESSION

S. 1093

To amend the patent law to restore the term of the patent grant in the case of certain products for the time of the regulatory review period preventing the marketing of the product claimed in a patent.

IN THE SENATE OF THE UNITED STATES

MAY 7 (legislative day, APRIL 15), 1985

Mr. MATHIAS (for himself, Mr. THURMOND, Mr. BIDEN, Mr. DOLE, Mr. DECONCINI, Mr. HEFLIN, Mr. DENTON, and Mr. SPECTER) introduced the following bill; which was referred to the Committee on the Judiciary

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A BILL

To amend the patent law to restore the term of the patent grant in the case of certain products for the time of the regulatory review period preventing the marketing of the product claimed in a patent.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act may be cited as the "Agricultural Patent Reform Act of 1984".

SEC. 2. (a) Title 35 of the United States Code is amended by adding the following new section immediately after section 156.

BEST COPY AVAILABLE

"§ 156. Restoration of patent term for certain agricultural and chemical products

"(a)(1) The term of a patent which claims a product subject to a regulatory review period or a method for using such a product or a method for manufacturing such a product shall be extended, in accordance with this section, from the original expiration date of the patent if—

"(A) the product sponsor gives notice to the Commissioner in compliance with the provisions of subsection (b)(1);

"(B) the product has been subject to a regulatory review period pursuant to statute before its commercial marketing or use;

"(C) the patent to be extended has not expired prior to notice to the Commissioner under subsection (b)(1);

"(D)(i) in the case of a patent which claims a method of manufacturing the product which does not primarily use recombinant DNA technology in the manufacture of the product—

"(I) no other patent has been issued to the patent owner which claims the product or a method of using the product; and

"(II) no other method of manufacturing the product which does not primarily use DNA technology in the manufacture of the product is covered by a claim in a patent issued to the patent owner having an earlier issuance date;

"(ii) in the case of a patent which claims a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product—

"(I) the holder of the patent for a method of manufacturing the product is not the holder of a patent for the product or for a method of using the product;

"(II) no other method of manufacturing the product primarily using recombinant DNA technology is covered by a claim in a patent having an earlier issuance date: and

"(III) the holder of the patent for a method of manufacturing is not owned or controlled by a holder of a patent for the product or for a method of using the product or by a person who owns or controls a holder of such a patent, and does not own or control the holder of such a patent or a person who owns or controls a holder of such a patent; and

"(E) except in the case of a patent which claims a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product, the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

"(2) The rights derived from any claim of any patent extended under paragraph (1) shall be limited in scope during the period of any extension as follows:

"(A) In the case of any patent, to the scope of such claim which relates to the product subject to regulatory review.

"(B) In the case of a patent which claims a product or a method of using a product—

"(i) which is subject to regulatory review under the Federal Food, Drug, and Cosmetic Act, to the uses of the product which may be regulated by the chapter of such Act under which the regulatory review occurred, or

"(ii) which is subject to regulatory review under any other statute, to the uses of the product which may be regulated by the statute under which the regulatory review occurred.

"(C) In the case of a patent which claims a method of manufacturing a product, to the method of manufacturing as used to make the approved product.

"(3)(A) Subject to subparagraph (B), the term of a patent shall be extended by the time equal to the regulatory review period which occurred during the period up to ten years after the date of filing of the earliest application for such patent and the time equal to one-half the regulatory review period which occurred during the period between ten and twenty years from the filing date of the earliest patent application for such patent.

"(B)(i) In determining a regulatory review period for purposes of subparagraph (A), if an application or notice described in paragraph (5)(B)(ii) or (5)(C)(ii) of subsection (c) was rejected and returned to the product sponsor because of insufficiency of data, the period beginning on the date the application was rejected for insufficiency of data and ending on the date the application was subsequently accepted shall be excluded, except that if during such period the product sponsor conducts a major health or environmental effects test, the period during which such test is conducted shall not be excluded. In determining the regulatory review period for purposes of subparagraph (A) with respect to a new animal drug, if the Secretary of Health and Human Services refuses to approve an application submitted under section 512 of the Federal Food, Drug, and Cosmetic Act on the grounds that the application contains insufficient information, the period beginning on the date the Secretary issues an order under subsection (d)(1) of such section refusing to approve such application and ending on the date a subsequent application is approved shall be excluded.

"(ii) In determining a regulatory review period for purposes of subparagraph (A), the regulatory review period shall be reduced by any period determined under subsection (b)(2) during which the applicant for the patent extension did not act with due diligence.

"(iii) In no event shall the term of any patent be extended for more than five years. No term of any extended patent may exceed twenty-five years from the date of filing of the earliest United States patent application which provides support under section 120 of this title for any claim of the patent to be extended. If the regulatory review period for a product began before the date of enactment of this section and if on such date the regulatory review period has not ended, the period of patent extension for the patent which claims the product or a method of using or manufacturing the product shall be measured from the date of enactment and shall not exceed three years.

"(C) In no event shall more than one patent be extended for the same regulatory review period for any product.

"(D) In the case of a pesticide, all formulations of such pesticide containing the identical active ingredient shall be considered the same pesticide and no pesticide may be the subject of more than one patent extension.

"(b)(1) To obtain an extension of the term of a patent under subsection (a), the product sponsor shall notify the Commissioner under oath, within ninety days after the termination of the regulatory review period for the product to which the patent relates, that the regulatory review period has ended. If the product sponsor is not the owner of record of the patent, the notification shall include the written consent of the owner of record of the patent to the extension. Such notification shall be in writing and shall—

"(A) identify the Federal statute under which regulatory review occurred or, if the regulatory review occurred under the Federal Food, Drug, and Cosmetic Act, the chapter of the Act under which the review occurred;

"(B) state the dates on which the regulatory review period commenced and ended;

"(C) identify the product for which regulatory review was required;

"(D) state that the requirements of the statute under which the regulatory review referred to in subsection (a)(1)(B) occurred have been satisfied and commercial marketing or use of the product is not prohibited; and

"(E) identify the patent and any claim thereof to which the extension is applicable; the date of filing of the earliest application for the patent; and the length of time of the regulatory review period for which the term of such patent is to be extended; and state that no other patent has been extended for the regulatory review period for the product.

"(2)(A) Within 60 days of the submittal of the extension notice under paragraph (1), the Commissioner shall notify—

"(i) the Secretary of Agriculture if the patent claims a veterinary biological product subject to the Virus-Serum-Toxin Act or a method of using or manufacturing such a product,

"(ii) the Secretary of Health and Human Services if the patent claims an animal drug product or animal antibiotic product subject to the Federal Food, Drug, and Cosmetic Act or a method of using or manufacturing such a product,

"(iii) the Administrator of the Environmental Protection Agency if the patent claims a pesticide subject to the Federal Insecticide, Fungicide, and Rodenticide Act, a chemical substance or mixture subject to the Toxic Substances Control Act, or a method of using or manufacturing such a pesticide, substance, or mixture, of the extension notice and shall submit to the Secretary or Administrator who is so notified a copy of the extension notice. Not later than thirty days after the receipt of the extension notice from the Commissioner, the Secretary or Administrator receiving the extension notice shall review the dates contained in such notice pursuant to paragraph (1)(B) and determine the applicable regulatory review period, shall notify the Commissioner of the determination, and shall publish in the Federal Register a notice of such determination.

"(B) If a petition is submitted to the Secretary or Administrator making the determination under subparagraph (A), not later than one hundred and eighty days after the publication of the determination under subparagraph (A), upon which it may reasonably be determined that the product sponsor did not act with due diligence during the applicable regulatory review period, the Secretary or Administrator making the determination shall, in accordance with regulations promulgated by such Secretary or Administrator, determine if the product sponsor acted with due diligence during the applicable regulatory review period. The Secretary or Administrator shall make such determination not later than 90 days after the receipt of such a petition. The Secretary of Health and Human Services may not delegate such authority to make the determination prescribed by this subparagraph to an office below the Office of the Commissioner of Food and

Drugs, the Secretary of Agriculture may not delegate such authority to an office below the Deputy Administrator of Veterinary Services, and the Administrator of the Environmental Protection Agency may not delegate such authority to an office below the Assistant Administrator for Pesticides and Toxic Substances.

"(C) The Secretary or Administrator making a determination under subparagraph (B) shall notify the Commissioner of the determination and shall publish in the Federal Register a notice of such determination, together with the factual and legal basis for such determination. Any interested person may request, within the 60-day period beginning on the publication of a determination, the Secretary or Administrator making the determination to hold a hearing on the determination. Such a hearing shall be an informal hearing which is not subject to section 554, 556, or 557 of title 5, United States Code. If such a request is made within such period, such Secretary or Administrator shall hold such hearing not later than thirty days after the date of the request, or at the request of the person making the request, not later than sixty days after such date. The Secretary or Administrator who is holding the hearing shall provide notice of the hearing to the product sponsor and to any interested person and provide the owner and any interested person an opportunity to participate in the hearing. Within thirty days after the completion of the hearing, such Secretary or Administrator shall affirm or revise the determination which was the subject of the hearing and notify the Commissioner of such affirmation or any revision of the determination and shall publish such affirmation or revision in the Federal Register.

"(D) Failure of a product sponsor to act with due diligence during a regulatory review period shall not be a defense in any action involving the infringement of a patent.

"(E) For purposes of this paragraph, the term 'due diligence' means that degree of attention, sustained directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period.

"(F) In a proceeding under this paragraph, the Secretary and Administrator may take into consideration the failure of a product sponsor to submit data which the product sponsor knew or reasonably should have known was necessary to support an application or notice described in paragraph (5) of subsection (c).

"(G) The Secretary and the Administrator may establish such fees as the Secretary and Administrator determine appropriate to cover the costs to the Secretary and the Administrator of making the review under subparagraph (A), receiving and acting upon petitions under subparagraph (B), and holding hearings under subparagraph (C).

"(3) Upon receipt of a final determination of the applicable regulatory review period under paragraph (2), the Commissioner shall issue to the owner of record of the patent a certificate of extension, under seal, stating the fact and length of the extension, identifying the product and the statute under which regulatory review occurred, and specifying any claim to which such extension is applicable. Such certificate shall be recorded in the official file of the patent so extended and shall be considered as part of the original patent. The Commissioner shall publish in the Official Gazette of the Patent and Trademark Office a notice of such extension.

"(4) If information submitted by a product sponsor during a regulatory review period is considered as trade secret or confidential commercial or financial information under the law under which such regulatory review occurred, such information may only be disclosed under this section in accordance with such law.

"(c) As used in this section:

"(1) The term 'product' means any machine, manufacture, or composition of matter for which a patent may be obtained and is limited to the following:

"(A) Any new animal drug or animal antibiotic subject to regulation under the Federal Food, Drug, and Cosmetic Act.

"(B) Any veterinary biological product subject to regulation under the Virus-Serum-Toxin Act.

"(C) Any pesticide subject to regulation under the Federal Insecticide, Fungicide, and Rodenticide Act.

"(D) Any chemical substance or mixture subject to regulation under the Toxic Substances Control Act.

"(2) The term 'major health or environmental effects test' means an experiment or study to determine or evaluate health or environmental effects which requires at least six months to conduct, not including any period for analysis or conclusions, and the data from which is submitted to receive permission for commercial marketing or use.

"(3) The term 'earliest application for the patent' means the patent application providing the earliest benefit of a filing date to the patent and includes patent applications under section 120.

"(4) The term 'product sponsor' means any person who, with the consent of the patent owner, initiates testing or investigations, claims an exemption, or submits an application, petition, protocol, request, or notice described in paragraph (5) of this subsection.

"(5) The term 'regulatory review period' has the following meaning:

"(A) With respect to a product which is a new animal drug, animal antibiotic, or veterinary biological product, the regulatory review period is the sum of—

"(i) the period beginning on the date—

"(I) an exemption under subsection (j) of section 512 of the Federal Food, Drug, and Cosmetic Act, or

"(II) the authority to prepare an experimental biological product under the Virus-Serum-Toxin Act,

became effective for the approved product and ending on the date an application was submitted for such product under section 512 of the Federal Food, Drug, and Cosmetic Act or the Virus-Serum-Toxin Act, and

"(ii) the period beginning on the date the application was submitted for the approved product under section 512 of the Federal Food, Drug, and Cosmetic Act or the Virus-Serum-Toxin Act and ending on the date such an application was approved.

"(B) With respect to a product which is a pesticide, the term means the sum of—

"(i) the period beginning on the earlier of the date the product sponsor (I) initiates a major health or environmental effects test on such pesticide, or (II) requests, in accordance with regulations issued by the Administrator, the grant of an experimental use permit for the pesticide under section 5 of the Federal Insecticide, Fungicide, and Rodenticide Act, and ending on the date an application is submitted for registration of such pesticide pursuant to section 3 of such Act, and

"(ii) the period beginning on the date an application is submitted, in accordance with regulations issued by the Administrator, for registration of such pesticide pursuant to section 3 of such Act and ending on the date such pesticide is first registered, either conditionally or fully, under such section.

"(C) With respect to a product which is a chemical substance for which notice is required under section 5 of the Toxic Substances Control Act or which is a mixture which contains a substance for which such notice is required and—

"(i) which is subject to a rule requiring testing under section 4(a) of such Act, the term means a period commencing on the date the product sponsor has initiated the testing required in such rule and ending on the expiration of the notice period for such chemical substance or mixture under section 5 of such Act, or if an order or injunction is issued under section 5(e) or 5(f) of such Act, the date on which such order or injunction is dissolved or set aside; or

"(ii) which is not subject to a testing rule under section 4 of such Act, the term means a period commencing on the earlier of the date the product sponsor—

"(I) submits, in accordance with regulations issued by the Administrator, a notice under section 5 of such Act, or

"(II) initiates a major health or environmental effects test on such chemical substance or mixture,

and ending on the expiration of the notice period for such substance under section 5 of such Act or if an order or injunction is issued under section 5(e) or 5(f) of such Act, the date on which such order or such injunction is dissolved or set aside.

No regulatory review period shall be deemed to have commenced until a patent has been granted for the product which is subject to regulatory review, for the method for using such product, or for the method for producing such product.

"(6) The term 'Virus-Serum-Toxin Act' means the Act of March 4, 1913 (21 U.S.C. 151–158).".

(b) The analysis for chapter 14 of title 35 of the United States Code is amended by adding at the end the following:

"157. Restoration of patent term for certain agricultural and chemical products.".

Senator **Mathias**. With that in mind, we will keep the hearing record open for 1 month to allow for additional submissions from the witnesses and written testimony from any other interested parties. And in order that we can hear all of the witnesses today, I am going to ask that they confine oral presentations to 5 minutes, though their full written statements will be printed in the record as if delivered in full.

In that connection, the Environmental Protection Agency and the Federal Food and Drug Administration were unable to send spokesmen today but, as I said, plan to submit written statements. The administration will be represented today by the Patent and Trademark Office.

We will begin this morning, then, with the Patent and Trademark Office, the Honorable Donald J. Quigg, the Acting Commissioner.

Commissioner, before you testify, let me call on the Senator from Ohio.

OPENING STATEMENT OF HON. HOWARD M. METZENBAUM, A U.S. SENATOR FROM THE STATE OF OHIO

Senator **Metzenbaum**. Thank you, Mr. Chairman.

Mr. Chairman, I have the greatest respect for you, as you well know; we have worked together on any number of matters during the years we have served together in the U.S. Senate. But I am frank to say that I have some very serious doubts about this bill.

In my view, Congress made a mistake last year in passing the drug patent extension bill. As a result of the passage of that bill, consumers will pay hundreds of millions of dollars for it. It is my view that this bill is even worse, because as a matter of fact, the terms of this bill are worse than the drug patent extension bill, but it should be pointed out that there was sort of a quid pro quo; there was an argument as to why that bill made sense, even though I am frank to say that I, personally, think the price is too high a price to pay. And that is because it permitted a greater sale and utilization of generic drugs.

In this instance, I see no particular advantage to the American people. I see it as inflationary legislation. I think the farm groups that have come in to say that they do not oppose or they support it, whatever the case, have been misled, because as far as I can see in my years here in this body and my tenure as chairman of the Antitrust Committee, every time you eliminate competition, you drive up the prices to those who use the product. And that means you drive up the prices to the farmer.

Therefore, I am hard pressed to understand how any farm group can come in here speaking for the American farmer, who is having a tough enough time at the present instance in keeping from losing his or her farm, how they can say that they are for this bill which, no question, will mean millions of more dollars that will be paid to the chemical companies for their agricultural products.

The record shows that prices can drop by as much as 50 percent if competition is allowed. And if you do not have competition because of an extension of the patent, somebody is going to pay the price, the price to the American farmer and, indirectly, the price that will be paid by the American consumer.

So I do not understand why this bill makes good sense. According to a 1982 Department of Agriculture study, pesticides account for 7½ percent of farm production costs. Farmers spend about $4,300,000,000 a year in the United States for pesticides. And if you increase that amount by hundreds of millions or billions, it is going to come out of somebody's pocket, not the chemical company's. It is going to go into the chemical company's pocket.

The chemical companies claim they need a longer monopoly to recover the costs of research and that research will suffer without patent extension. But the record shows that research and development expenditures as a percentage of sales is going up under the present laws, not down; a large number of new products have been developed in the last few years, and the major companies did well last year. In the industry, economic outlook is good. So why do we need this bill? It will drive up prices.

Every indication is that the industry is healthy and incentives for research are adequate at the present time. There is not much question about the fact that this is not an area where you have a lot of competition existing. The industries are concentrated, according to an FTC study: 90 percent of the corn herbicides are produced by four companies; 67 percent of the cotton herbicides are produced by two companies; 66 percent of sorghum herbicides are produced by one company. So why give more monopoly power to firms that are already highly concentrated?

This bill, like so many others that we handle in the Congress, has the attention and the support of the industry. And I look out in the audience and I see who is present, and I know hardly a face in that audience. But I would be willing to bet all the tea in China that very few of them speak for the American farmer unless they may in some instances speak for the American corporate farmers which have their own agenda.

The farmers of this country do not realize what is happening. The consumers of this country do not appreciate what is in this bill. And, therefore, we find ourselves with a very respectable list of cosponsors of this legislation, very respectable. And those of us who are opposed to it and who feel they have to be convinced as to why it makes sense, we find that we are rather lone voices.

Fortunately, it is possible in this body to make a lone voice heard. And I would say, Mr. Chairman, that unless there is overwhelmingly convincing evidence that this is good for the American farmer and good for the American consumer, that I do not believe the U.S. Senate should pass a bill that is only good for the American chemical companies.

Senator MATHIAS. Thank you very much, Senator Metzenbaum. The Senator from Ohio expressed himself very eloquently and forcefully as he usually does. I do not think it is appropriate for me to respond.

I would suggest one semantic change in your presentation which I think might help your own understanding. I suggest, instead of calling this a patent extension bill, that it should properly be called a patent restoration bill, in that it merely gives back patent protection for the period of time which the Congress originally intended.

Senator METZENBAUM. In its being restored, will it actually be extended?

Senator MATHIAS. Many of the questions you raised, I think, will be answered during the course of the day. And if you stick with us through this hearing, I think we may extend your field of vision on the subject.

You may see more than you see right now.

Mr. Quigg, will you proceed.

STATEMENT OF HON. DONALD J. QUIGG, ACTING COMMISSIONER, PATENT AND TRADEMARK OFFICE, WASHINGTON, DC, ACCOMPANIED BY CHARLES E. VAN HORN, DIRECTOR, PATENT EXAMINING GROUP 120, ORGANIC CHEMISTRY AND BIOTECHNOLOGY, AND H. DIETER HOINKES, LAWYER, LEGISLATION AND INTERNATIONAL AFFAIRS, U.S. PATENT AND TRADEMARK OFFICE

Commissioner QUIGG. Mr. Chairman, Senator Metzenbaum. With me today at the table are Charles Van Horn and Dieter Hoinkes.

I welcome this opportunity to testify on the subject of patent term extension. Last year, Congress took the historic step of enacting the Drug Price Competition and Patent Term Restoration Act of 1984, which was strongly endorsed by the administration. That legislation, however, is limited mainly to human drug products and medical devices. Patentees in the areas of agricultural and industrial chemicals and animal drugs are subject to Federal premarket regulatory procedures, which are similar to those experienced by owners of pharmaceutical patents. As a consequence, their effective patent terms continue to be seriously diminished.

Inventions in agricultural and industrial chemical technologies heavily depend on patent protection. Development of such inventions is extremely costly, and yet their imitation is often simple and inexpensive. Many other inventions need far greater outlays of capital to duplicate, and they also may have a shorter commercial life before being overtaken by the advances of technology. Agricultural and industrial chemical inventions, on the other hand, often have a commercial life extending beyond the expiration of the patent term. A shortened, effective patent term lessens the incentive for industries to continue making large commitments toward research and development.

Effective patent protection is a necessary prerequisite to chemical research, given the enormous costs and risks involved. In this regard, S. 1093 would be a welcome addition to existing law. The administration, therefore, strongly supports the principle of patent term extension as provided by this bill for patented inventions in the areas of agricultural and industrial chemicals and animal drugs.

My prepared testimony goes into detail regarding specific suggestions we have on how to improve S. 1093. In general terms, our principal concern lies with the bill's potential for deterring our agricultural and industrial chemical industry from undertaking important research and development activities.

S. 1093, in effect, rations patent rights by denying extensions to a patent owner based on other patents which that person owns or controls or on the existence of earlier patents on related technologies. The bill also discourages patent owners from trying to find new uses for their patented products and may discourage further research on products using certain active ingredients.

In addition, the bill contains a number of other substantive problems. For example, S. 1093 uses a very complicated formula for determining the period for patent extension when its purposes could be achieved far more simply by counting the entire regulatory review period and placing a cap on it. It permits patent term extension for chemicals and drugs that receive approval for marketing prior to enactment of this legislation. It may place us in a potential violation of the Paris Convention for the protection of industrial property in the way it requires us to treat foreign priority dates. And it does not provide that duties of the commissioner in this area should be purely ministerial.

The bill also requires the Patent and Trademark Office to adopt different administrative procedures for processing pharmaceutical patent extension and agricultural chemical patents, unnecessarily raising the cost of administering extensions for the latter.

Finally, S. 1093 fails to reflect the administration's commitment to the principle that users of the patent system should pay for its operation. These problem areas in S. 1093 can be easily corrected; in most cases, either by incorporating parallel provisions from Public Law 98-417 or by deleting parallel provisions that, in our view, should not have been included in that statute.

Thank you.

Senator **MATHIAS**. Thank you, Commissioner.

Now, you have made a number of suggestions as to changes. If the committee determines that those changes would be desirable, can we count on your assistance in the necessary drafting?

Commissioner **QUIGG**. Yes, sir.

Senator **MATHIAS**. Senator Metzenbaum.

Senator **METZENBAUM**. Commissioner, how long does regulatory review last for a typical pesticide or an animal drug?

Commissioner **QUIGG**. It has been awhile since I have heard the actual figures; it runs, in my mind, as somewhere around 5 years.

Senator **METZENBAUM**. What steps should you or the FDA or the EPA take to speed it up, or any other regulatory review body, and what could Congress do to help in that process?

Commissioner **QUIGG**. Well, Senator, as far as the Patent and Trademark Office is concerned, we are somewhat without any ability to speed up that processing. As far as the patent itself is concerned, we are taking steps to reduce the time of pendency of an application in the Patent and Trademark Office to at least 18 months by 1987. But as far as the regulatory provisions where the FDA looks at the testing of materials, we really have no input to that.

Senator **METZENBAUM**. Commissioner, you are testifying for this bill on behalf of the Patent Office. Would you explain to me why the bill deals different with those products which do not primarily use recombinant DNA technology and those that do use recombinant DNA technology?

Commissioner **QUIGG**. Well, I cannot speak for the drafters of the bill. DNA is a fairly recent development. It is on the front cutting edge of technology. And I would gather that the drafters of the bill had tried to simply differentiate that from the more standard approaches that have been used in years gone by.

Senator METZENBAUM. Why?

Commissioner QUIGG. That I cannot tell you. I just do not know what the drafters had in mind.

Senator METZENBAUM. And yet the U.S. Government Patent Office comes here and says we want this bill. The administration supports this bill.

Commissioner QUIGG. Yes, sir.

Senator METZENBAUM. And is it not reasonable for us in the Congress to expect those in the U.S. Government who come here to support a piece of legislation to be able to explain to us, and I am frank to tell you that I do not understand it, and I remember when we had similar legislation 1 or 2 years ago, and I went to the sponsor and I said to him, "What the hell does that mean?" And I read him some of the language in the proposal. And I have difficulty in comprehending what the thrust is as to why the distinction between the two areas. There are other portions of this bill that I am not going to press you on because of limitations of times. But I am frank to say that I have difficulty in comprehending some aspects of this legislation, and I assume since the Patent Office is here supporting it that we could look to the Patent Office for some clarification on it.

If there is somebody else that you want to yield to, if this gentleman is an authority on the subject, I have no objection to his responding.

Commissioner QUIGG. Well, first of all, Senator, I would say that in our prepared testimony we have suggested some rather substantial changes be made to clarify the bill and simplify it. But I would ask if Mr. Hoinkes has anything, to let him answer.

Senator METZENBAUM. You are an assistant at the Patent Office, sir?

STATEMENT OF H. DIETER HOINKES

Mr. HOINKES. Yes, Senator.

If I may address the question you have asked, why there is a difference between the method of manufacture using recombinant DNA technology and a simple non-DNA type of method of manufacturing a product, the reason, as far as we can tell——

Senator METZENBAUM. Would you just repeat that sentence? Between using the recombinant DNA technology and a simple——

Mr. HOINKES [continuing]. Yes. Let me repeat that, if I may.

There is a distinction made in the manufacture of the product, one using recombinant DNA technology and another method not using recombinant DNA technology. And as far as the eligibility or extension of the patent is concerned, the bill makes a difference between using DNA recombinant technology and not using, depending on——

Senator METZENBAUM [continuing]. That is where we started off the question. We agree on that.

Mr. HOINKES. Exactly.

Now, from what I understand, the difference there is that in the last Congress when H.R. 3605 was pending, which covered both pharmaceuticals and agricultural chemicals, similar provisions were also incorporated in there, but the more restrictive ones were later removed. The theory behind them was that only new chemical entities should be entitled to an extension and that if you had a conventional method of manufacturing the product, you would not necessarily be entitled to an extension. However, if you had produced your product using recombinant DNA, even though there was already an earlier conventional method of producing the product, you would be entitled to an extension of the patent which claims a method of manufacture of the product using recombinant DNA. In other words, the idea behind it was that just because a product had been produced before by a conventional method ought not penalize the——

Senator **Metzenbaum**. Is that what the bill says now? I do not read it that way.

Mr. **Hoinkes** [continuing]. Well, in effect, if you take a look at sections 157 (a)(1)(D) and (a)(1)(E), you will find these distinctions made between using recombinant DNA and not using recombinant DNA. But as the Commissioner has stated, Senator Metzenbaum, we are not happy with the way this bill is phrased and have made suggestions as to how it could be improved.

Senator **Metzenbaum**. Well, I am not going to press the point, but I will say that I am not satisfied.

Mr. **Hoinkes**. Neither are we, Senator.

Senator **Metzenbaum**. Well, then, we will go on.

Senator **Mathias**. I believe that some of the questions that the Senator from Ohio has raised will be answered by some of the technical witnesses who will follow, and I think we can satisfy his curiosity on those questions very promptly.

Just as a matter of legislative history, let me say that Senate bill 1093 owes some of its origins and ideas to the work that was done in the House Judiciary Committee in an agricultural and animal drug bill that actually was reported by the committee last year. So these are not novel ideas; they are ideas that have been in the public domain for some time. The aim was to have a headstart in the other body after the Senate acted on the bill.

I think there is some difference of opinion within the industry as to the approach of Senate bill 1093 on recombinant DNA technologies. And, once again, I think that will become clear as the testimony unfolds.

Thank you very much for being with us, Commissioner. We will appreciate having your full statement which will all appear in the record.

Commissioner **Quigg**. Thank you.

[Prepared statement of Commissioner Quigg follows:]

PREPARED STATEMENT OF DONALD J. QUIGG

SUMMARY

Last year, Congress took the historic step of enacting the "Drug Price Competition and Patent Term Restoration Act of 1984", which was strongly endorsed by the Administration. That legislation, however, is limited mainly to human drug products and medical devices. It does not address the plight of inventors in the field of agricultural and industrial chemicals and animal drugs. Patentees in these areas of technology are subject to Federal premarket regulatory procedures which are similar to those experienced by owners of pharmaceutical patents. As a consequence, their effective patent terms continue to be seriously diminished.

S. 1093 would be a welcome addition to existing law. The Administration, therefore, strongly supports the principle of patent term extension as provided by this bill to patented inventions in the areas of agricultural and industrial chemicals and animal drugs. Due to a number of objectionable features, we cannot endorse S. 1093 as presently drafted. However, these problems can easily be corrected and the Administration would strongly endorse the bill, if amended along the lines suggested in my statement.

Our principal concern lies with the bill's potential for deterring our agricultural and industrial chemical industry from undertaking important research and development activities. This potential might be realized because S. 1093 in effect "rations" patent rights by denying extension to a patent owner based on other patents which that person owns or controls or on the existence of earlier patents on related technologies. The bill also discourages patent owners from trying to find new uses for their patented products and may discourage further research on products using certain active ingredients.

Further, S. 1093 uses a very complicated formula for determining the period of patent extension, when its purposes could be achieved far more simply by counting the entire regulatory review period and placing a cap thereon. It permits patent term extension for chemicals and drugs that receive approval for marketing prior to enactment. It may place us in potential violation of the Paris Convention for the Protection of Industrial Property in the way it requires us to treat foreign priority dates. It does not provide that the duties of the Commissioner in this area should be purely ministerial, and requires us to adopt different administrative procedures for processing pharmaceutical patent extensions and agricultural chemical patents, thereby unnecessarily raising the costs of administering extensions for the latter. Finally, S. 1093 fails to reflect the Administration's commitment to the principle that users of the patent system should pay for its operation.

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Mr. Chairman and Members of the Subcommittee:

I welcome this opportunity to testify on the subject of patent term extension which would improve our patent system by providing an equitable approach to the effective length of patent terms.

Last year, Congress took the historic step of enacting the "Drug Price Competition and Patent Term Restoration Act of 1984", which was strongly endorsed by the Administration. That legislation, however, is limited mainly to human drug products and medical devices. It does not address the plight of inventors in the field of agricultural and industrial chemicals and animal drugs. Patentees in these areas of technology are subject to Federal premarket regulatory procedures which are similar to those experienced by owners of pharmaceutical patents. As a consequence, their effective patent terms continue to be seriously diminished.

Inventions in agricultural and industrial chemical technologies heavily depend on patent protection. Development of such inventions is extremely costly, and yet their imitation is often simple and inexpensive. Many other inventions need far greater outlay of capital to duplicate, and they also may have a shorter commercial life before being overtaken by the advance of technology. Agricultural and industrial chemical inventions, on the other hand, often have a commercial life extending beyond the expiration of the patent term. Because a shortened effective patent term lessens the incentive for industry to continue making large commitments toward research and development, we need to move to insure that those incentives are restored. Effective patent protection is a necessary prerequisite to chemical research, given the enormous costs and risks involved. In this regard, S. 1093 would be a welcome addition to existing law. The Administration, therefore, strongly supports the principle of patent term extension as provided by this bill to patented inventions in the areas of agricultural and industrial chemicals and animal drugs. Due to a number of objectionable features, we cannot endorse S. 1093 as presently drafted. However, these problems can easily be corrected and the Administration would strongly endorse the bill, if amended along the lines suggested in my statement.

Although S. 1093 is patterned on the patent term extension provisions of Public Law 98-417, now part of title 35, United States Code, it is in many instances different. In this regard it reflects the fact that it once was part of an earlier bill in the last Congress which addressed patent term extension for both pharmaceuticals and agricultural chemicals and was separated from that bill during early stages of Congressional consideration. As a consequence, some of the features of that earlier bill which were subsequently deleted or otherwise amended prior to enactment, have remained in S. 1093. Other parts of the earlier bill which were enacted despite opposition by this Administration have also been retained in S. 1093. And finally, some desirable features found in P.L. 98-417 have not been incorporated into this legislation. Specifically we have the following comments on S. 1093:

Section 157(a)(1)(D) of S. 1093 provides a complicated formula for determining a patent's eligibility for extension if it claims a method for manufacturing a product. A distinction is made between patents claiming a conventional process and those which claim the use of recombinant DNA technology. In each instance, the owner of the process patent is precluded from owning a patent for the product or for a method of using the product. In addition, a conventional process patent is not eligible for extension if the owner was issued an earlier patent claiming another conventional process of manufacturing the product. In the case of a patent claiming the use of recombinant DNA technology, that patent is only eligible for extension if no earlier patent exists, regardless of ownership, claiming the use of recombinant DNA technology in the manufacture of the product.

This approach is unfair. A newly discovered process for making a product may well represent a scientific and commercial breakthrough. The owner of a patent claiming such a process should not be denied extension of a patent on the basis of other patents he owns or controls, nor should the existence of earlier patents to related technologies have any bearing on the merits of extending a particular process patent which was denied a full and effective term due to Federal premarket regulatory review.

This is not the first time that the Senate has considered and rejected this approach. During the 98th Congress, a similar approach was contained in an early version of the "Drug Price Competition and Patent Term Restoration Act of 1984" (S. 2748), but the provision was omitted in the bill as passed by the Senate (S. 1538), and as finally enacted into law (P.L. 98-417). We urge that S. 1093 be modified to omit the complicated formula appearing in section 157(a)(1) (D), and that the simpler and fairer approach of 35 U.S.C. 156(a)(5) (B) be adopted.

Section 157(a)(1)(E) permits, with one exception, extension for patents relating to products or their use only if the regulatory review resulted in the first permitted commercial marketing or use. The exception exempts patents claiming a method of manufacturing products with the use of recombinant DNA technology. We question the wisdom of this policy that would deny extension to later patents which disclose, for example, new and unobvious uses for a previously approved product. Such a policy does not lend encouragement to the owner of a product patent to invest the sums needed for research and development to find new uses for his already patented product. It would seem desirable to allow patent term extension for subsequent patents which disclose new use inventions.

Sections 157(a)(3)(A) and (B)(iii) would establish a formula for the length of time for which a patent term may be extended. For regulatory review during the first ten years from the filing date of the earliest patent application, full credit would be given toward patent term extension. Between ten and twenty years from that filing date, only half the regulatory review period would count toward extension. Finally, no term could exceed 25 years from the earliest filing date of the application. Since S. 1093 already contains a five-year cap of maximum allowable patent term restoration, we would prefer the simpler approach of counting the full regulatory review period up to a fixed number of years toward obtaining an extension of the patent term. This is especially so, since the formula expressed in section 157(a)(3)(A) --taking into account regulatory review periods for patent term extension before any patent has issued-- is apparently contradicted by the last sentence of section 157(c)(5), which states that no regulatory review period shall be deemed to have commenced until the patent to be extended has been granted.

Further, section 157(a)(3)(A) refers to "the date of filing of the earliest application" which triggers the running of the first ten-year period. This date is defined in section 157(c)(3) as being the one "providing the earliest benefit of a filing date to the patent and includes patent applications under section 120". This definition, however, is not limited to applications under section 120 and, therefore, includes foreign priority filings. Such a requirement may be in conflict with the Paris Convention for the Protection of Industrial Property, which provides that a foreign priority date may not be considered in the allocation of the length of a patent term. Accordingly, we prefer the definition of the earliest application for a patent to be the same as that spelled out in section 157(a)(3)(B)(iii) of the bill, namely, "the earliest United States patent application which provides support under section 120 of this title for any claim of the patent to be extended".

Section 157(a)(3)(B)(iii) is unclear in several other aspects. The third sentence telescopes the concepts of patent term extension and regulatory review period into one. To avoid confusion, we would suggest the following wording as a substitute: "If the regulatory review period for a product began before the date of enactment of this section and if on such date the regulatory review period has not ended, it shall be measured from the date of enactment and the period of extension for the patent shall not exceed three years." Further, the legislation should also clarify how patents should be treated for which such review ended before enactment. The present wording of this section would permit the same length of patent term extension for these patents as it would provide for patents for which the regulatory review period began only after the date of enactment. This is not consistent with the bill's less generous treatment of patents for which regulatory review began but did not end before enactment.

Another point concerns the language of section 157(a)(3)(D). This section is unclear as to whether it would provide patent term extension for a product having two or more active ingredients where only one of these ingredients had been claimed in a previously extended patent. We believe it would be unwise to deny patent term extension to compositions with multiple active ingredients solely on the basis that one of those ingredients was protected by a patent which had already been extended. The product covered by the previously extended patent can be used by all upon expiration of the patent. To deny patent extension to another product simply because it includes one ingredient which was claimed in an earlier extended patent would serve as a disincentive to further research on products using that ingredient -- a result contrary to the purposes of the bill.

An important consideration concerns the duties of the Commissioner of Patents and Trademarks under this legislation. For example, section 157(b)(3) requires the Commissioner to specify in the certificate of extension any claim to which such extension is applicable. Although the product sponsor is required by section 157(b)(1)(E) to identify in the notification the particular claim involved, we would prefer section 157(b)(3) to state that, when issuing a certificate, the Commissioner may rely solely on the information contained in the notification referred to in section 157(b)(1). Such language would clearly reflect that the Commissioner's duties are purely ministerial. This change would considerably reduce the costs to the Office to administer patent term extension applications in the field of agricultural and industrial chemicals. Further, false information furnished by the applicant for extension could be used as a defense to defeat any infringement action by the owner of the extended patent. And lastly, section 156(e) of title 35, United States Code, already addresses these duties of the Commissioner when issuing a certificate of extension for pharmaceutical patents.

It would be in the interest of the public, as well as in the interest of Federal agencies and departments involved in the administration of patent term extension, if procedural aspects of legislation providing for extension of agricultural chemical patents were harmonized to the extent possible with existing law providing for extension of pharmaceutical patents. In some instances, applicants for extension of pharmaceutical patents are the same as those applying for extension of agricultural chemical patents. Procedural uniformity would certainly lessen the burden on applicants and agencies alike.

For example, in detailing the elements which an application for extension of a patent relating to a human drug product shall contain, section 156 (d)(1)(E) of title 35, United States Code, provides for the furnishing of the patent or other information as the Commissioner may require. Further, 35 U.S.C 156 (d)(4) provides that "[a]n application for the extension of the term of a patent is subject to the disclosure requirements prescribed by the Commissioner". It would be useful to add such provisions also to the requirements of what a notification for extension under section 157 (b)(1) should contain, in order to assist the Commissioner in carrying out his duties.

Finally, we note that section 157(b)(2)(G) permits the Secretary and the Administrator to establish fees to cover the costs involved in carrying out their duties under this bill. Although the duties of the Commissioner of Patents and Trademarks may not be as extensive as those of the Secretary and the Administrator, we urge that the Commissioner also be authorized to establish fees covering the costs of processing notifications for patent term extension. Such an authorization is consistent with the policy of charging the users of the patent system with the costs for its administration and, incidentally, is also included in 35 U.S.C. 156(h), in the case of applications for pharmaceutical patent extentions.

Each of these problem areas in S. 1093 can be easily corrected, in most cases either by incorporating parallel provisions from Public Law 98-417 or by deleting parallel provisions that, in our view, should not have been included in that statute.

Senator **Mathias**. We will now ask for a panel of witnesses: The Honorable Wayne A. Cawley, secretary of agriculture of the Free State of Maryland; Mr. Henry Holloway, president of the Maryland Farm Bureau—Senator Metzenbaum, you wanted to meet a farmer—and Mr. Jack Early, president of the National Agricultural Chemicals Associations. I understand that Vaughn Bryson will also accompany them.

Mr. Secretary, would you lead off?

I think all of you are familiar with our traffic system here. We will give you the green light when you start; when you see the red light, why, that means what it usually means, it is time to stop.

STATEMENT OF A PANEL, CONSISTING OF HON. WAYNE A. CAWLEY, JR., SECRETARY OF AGRICULTURE, MARYLAND DEPARTMENT OF AGRICULTURE, ANNAPOLIS, MD; HENRY HOLLOWAY, PRESIDENT, MARYLAND FARM BUREAU, RANDALLSTOWN, MD; JACK EARLY, PRESIDENT, NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION, WASHINGTON, DC, ACCOMPANIED BY VAUGHN D. BRYSON, PRESIDENT, ELANCO PRODUCTS, DIVISION OF ELI LILLY CORP., INDIANAPOLIS, IN; AND EDWIN TOCKER, SENIOR ATTORNEY WITH E.I. DU PONT DE NEMOURS & CO., CHAIRMAN OF NACA'S PATENT COMMITTEE

Mr. **Cawley**. Mr. Chairman, members of the committee, I would like to thank you for allowing me the opportunity to testify before you today in support of Senate bill 1093, the Agricultural Patent Reform Act of 1985.

My name is Wayne A. Cawley, Jr., and I am Maryland's secretary of agriculture and a farmer from Caroline County, MD, which happens to be on the Eastern Shore of Maryland.

The Patent Reform Act was brought to my attention by my advisory group, the Maryland Agricultural Commission, which has 17 members representing every major commodity group in Maryland. The commission recommended that I support this legislation. Now, when 17 agricultural leaders representing diverse interests vote unanimously, and I emphasize, vote unanimously on an agricultural issue, this secretary listens. I believe that the patent reform legislation will increase the amount of money that is invested in agricultural chemical research and thereby improve the efficiency and safety of the chemicals used in agriculture.

With considerable support from yourself, Mr. Chairman, the Chesapeake Bay is on its way to recovery. Gov. Harry Hughes has invested large sums of Maryland taxpayers' money on cleaning up the Chesapeake Bay, and although agricultural chemicals were not cited as a problem by the EPA, Chesapeake Bay reports much attention has been placed upon them, with several bills being presented before the Maryland General Assembly in 1985 to control their use.

We need more research to evaluate existing chemicals and to develop new chemicals. And I believe that by offering equal patent terms for agricultural chemicals, as for other regulated and nonregulated products, you will be doing a great service to the citizens of this country as well as to the starving populations of other countries.

Agriculture in Maryland is its largest industry; it is the largest industry in the whole United States, and yet, still only 3 percent of the population are providing the food for the remainder. This tremendous accomplishment has been achieved by improving efficiency through improved mechanization, improved genetics and improved agricultural chemicals.

Mr. Chairman, members of the committee, Maryland agriculture encourages you to pass Senate bill 1093.

Thank you.

I do have copies here, Mr. Chairman, that I will leave.

Senator **MATHIAS**. Thank you very much, Mr. Secretary.

[Statement of Mr. Cawley follows:]

PREPARED STATEMENT OF WAYNE A. CAWLEY, JR.

Mr. Chairman, members of the committee, I would like to thank you for allowing me the opportunity to testify before you today in support of Senate bill 1093—the Agricultural Patent Reform Act of 1985.

My name is Wayne A. Cawley, Jr., and I am Maryland's secretary of agriculture and a farmer from Caroline County.

The Patent Reform Act was brought to my attention by my advisory group—the Maryland Agricultural Commission, which has 17 members representing every major commodity group in Maryland. The Commission recommended that I support this legislation. When 17 agricultural leaders, representing diverse interests, vote unanimously on an agricultural issue—I listen. I believe that the patent reform legislation will increase the amount of money that is invested in agricultural chemical research and thereby improve the efficiency and safety of the chemicals used in agriculture.

With considerable support from you, Mr. Chairman, the Chesapeake Bay is on its way to recovery. Governor Hughes has invested large sums of Maryland taxpayer's money on cleaning up the Chesapeake Bay, and although agricultural chemicals were not cited as a problem by the EPA Chesapeake Bay reports, much attention has been placed upon them. Several bills were presented to the Maryland General Assembly in 1985 to control their use. Environmental groups and others are concerned about agricultural chemicals. For these reasons, we need more research to evaluate existing chemicals and to develop new chemicals. I believe that by offering equal patent terms for agricultural chemicals, as for other regulated and nonregulated products, you will be doing a great service to the citizens of this country as well as to the starving populations of other countries.

Agriculture is Maryland's largest industry—it is the largest in the whole of the United States and yet still only 3 percent of the population are providing the food for the remainder. This tremendous accomplishment has been achieved by more and greater efficiency through improved mechanization, improved genetics, and improved agricultural chemicals.

Mr. Chairman, members of the committee, Maryland agriculture encourages you to pass Senate bill 1093. Thank you.

If you have any questions, I will be pleased to try to answer them.

STATEMENT OF HENRY HOLLOWAY

Mr. **HOLLOWAY**. Mr. Chairman, members of the committee, I am Henry Holloway, president of Maryland Farm Bureau, a voluntary membership organization of 14,000-plus families.

We support Senate bill 1093.

This legislation should benefit consumers as much as farmers and ranchers who produce their food. The American public continues to demand and expect a generous supply of high quality, tasty foods. Until scientific research provides alternative methods of controlling insects, diseases and weeds, agricultural producers need protective products.

Regulatory agencies are gradually removing effective products from use, and farmers fear that those products will not be replaced. Senate bill 1093 should provide incentive for research and development of new patents.

As a beef, pork, and grain producer, I am personally aware of the need for, and importance of, agricultural chemicals.

We urge you to support 1093.

Senator **Mathias**. Thank you very much, Mr. Holloway.

STATEMENT OF JACK EARLY

Dr. **Early**. I am Jack Early, president of the National Agricultural Chemicals Association. Accompanying me this morning is Mr. Vaughn Bryson, president of Elanco Products Co., and immediately behind me is Mr. Edwin Tocker, a senior patent attorney with the Du Pont Co.

Mr. Chairman, the National Agricultural Chemicals Association is a nonprofit trade association representing approximately 100 companies which manufacture and formulate virtually all of the agricultural chemical products in the United States.

Mr. Chairman, we appreciate the opportunity this morning to testify and wish to state our very strong support for S. 1093, the Agricultural Patent Reform Act of 1985. This legislation will go far toward restoring patent life lost to agrichemical producers as a result of federally mandated testing and review required for the registration of our products. The 98th Congress acted when the pharmaceutical industry raised a similar concern. We hope the 99th Congress will also address the needs of the agrichemicals industry.

The essential point I wish to make, Mr. Chairman, is that the issue is basically and simply a matter of equity. Congress intended that a 17-year patent be awarded to promote the development of new technology, thereby encouraging the early disclosure of an invention while affording protection for the inventor. Since the adoption of the patent incentive system of 1790, there have been tremendous changes in the scientific knowledge in general and in the field of agriculture specifically, and developments should continue to be encouraged.

But while unregulated patented products are free to receive a full 17 years of patent protection, all agrichemical products are subject to Federal regulatory requirements which typically prevent them from receiving their full 17 years. Our experience shows that the average time for completion of testing and the regulatory review process for agricultural chemicals is 5 to 7 years from the time the patent is granted. Thus, agricultural chemicals are realizing far less patent protection than the Congress has originally intended in 1790.

In addition, passage of S. 1093 would accomplish four other important objectives. No. 1, it would sustain the incentive needed for agricultural chemical companies to continue to invest long-term, high-risk capital in research and development.

Second, the bill would help to reverse the current trend of fewer and fewer new and improved agrichemicals reaching the marketplace due to the increasing time from discovery to commercial use.

Third, the measure would help assure the availability of safer new agrichemicals indispensable for doubling our food production by the year 2030 to feed a world population estimated to grow to 8 billion by that time.

Fourth, the legislation would enable the U.S. agricultural chemical producers to maintain their leadership position internationally.

Conversely, Mr. Chairman, failure to enact S. 1093 would be a decided negative for this industry and American agriculture. As members of this committee and, indeed, the Congress know full well, the Nation's farmers are in perhaps the most dire straits since the Depression. Some fear the actual condition of the American agriculture may be even worse than that.

As you have indicated in your opening statement, Mr. Chairman, we are pleased to see that some 20-odd agricultural organizations such as the Farm Bureau, the Cotton Council, the wheatgrowers, and many others have indicated their support for this legislation. For the past several years, we have witnessed an ever-increasing time requirement for product testing to ensure that there are no unreasonable toxic effects from these compounds on either human health or the environment. The agricultural chemical industry totally agrees with these objectives. We want the day to come when no questions or fears will be raised about the use of our product.

Mr. Chairman, if it were not for the patent system, there would be fewer financial risks taken by this industry which would require substantial economic risk under the best of circumstances. Without the patent system, there simply would be fewer developments in the agricultural technology by private industry in this country.

Financial uncertainties have been illustrated in several ways. For example, it takes something like 12,000 chemicals tested by a company before they arrive at a chemical that would give you a marketable product. And that would invest something like $40 million to put that product on the market. These expenditures are large and extensive, and the erosion of some 5 to 7 years of our patent life makes a tremendous disincentive, Mr. Chairman, for our companies to invest in research and development

Before closing, Mr. Chairman, I would like to mention that this legislation is again before the Senate after having been passed last year, as you indicated. And you also indicated in your opening statement, Mr. Chairman, that last year certain issues groups opposed this legislation in order to achieve legislative changes in the pesticide law, FIFRA, we refer to it. We are currently negotiating with these groups in a coalition of environmental, consumer, and labor organizations to respond to their concerns in amending FIFRA.

Mr. Chairman, this concludes our presentation of testimony. We would be glad to respond to any questions you may have.

Thank you.

Senator MATHIAS. Thank you very much, Dr. Early.

[Statement and additional comments of Mr. Early follow:]

PREPARED STATEMENT OF THE NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION

SUMMARY OF ORAL TESTIMONY

- NACA strongly supports the bill.

- The essential issue is restoration of equity. Producers of agricultural chemicals lose five to seven years of patent protection due to Federal regulatory requirements.

- S. 1093 would sustain the initiative needed for agricultural chemical companies to continue to invest long-term, high-risk capital in R&D.

- The bill would help reverse the current trend of fewer and fewer new and improved agrichemicals reaching the marketplace due to the increasing time from discovery to commercial use.

- The measure would help assure the availability of safer new agrichemicals indispensable for the doubling of food production by the year 2030 to feed a world population estimated to grow to 8 billion.

- The legislation would enable U.S. producers to maintain their international leadership position.

- Agriculture, now in dire straits, requires newer and better products which can come only from a vigorous industry possessing strong innovation. Innovation cannot come from a technologically-intensive industry whose incentives are less than its unregulated counterparts.

- On the average, it now takes up to $40 million to bring a new product from discovery to market. If a new manufacturing facility is required -- and more often then not it is -- an additional $40 - $70 million may be necessary.

- Without adequate patent protection, agchem companies will be less able to undertake the increasingly costly and time-consuming research involved in discovering and developing new technology.

* * * * *

I am Jack D. Early, President of the National Agricultural Chemicals Association (NACA). Accompanying me are Mr. Vaughn Bryson, President of Elanco Products Company, a Division of Eli Lilly and Company, and Mr. Edwin Tocker, Senior Attorney with E. I. du Pont de Nemours & Company, and Chairman of NACA's Patent Committee.

The National Agricultural Chemicals Association is a nonprofit trade association representing approximately 100 companies which manufacture or formulate virtually all of the agricultural chemical products in the United States. These pesticides or "agrichemicals" include insecticides, fungicides, bactericides and herbicides. Broadly speaking, our companies' products are those chemicals which are used to protect crops from destruction by various insects, diseases and weeds.

Mr. Chairman, we appreciate this opportunity to testify and wish to state our very strong support for S. 1093, the Agricultural Patent Reform Act of 1985. This legislation will go far toward restoring patent life lost to agrichemical producers as a result of Federally mandated testing and review required for the registration of our products. The 98th Congress acted when the pharmaceutical industry raised a similar concern. We hope the 99th Congress will also address the needs of the agrichemicals industry.

The essential point I wish to make, Mr. Chairman, is that the issue is basically and simply a matter of equity. Congress intended that a 17-year patent be awarded to promote the development of new technology, thereby encouraging the early disclosure of an invention while affording protection for the inventor. Since the adoption of the patent incentive system in 1790, there have been tremendous changes in scientific knowledge in general and in the field of agriculture specifically -- and developments should continue to be encouraged.

But while unregulated patented products are free to receive the full 17 years of patent protection, all agrichemical products are subject to Federal regulatory requirements which typically prevent them from receiving the full 17 years. Our experience shows that the average time for completion of testing and the regulatory review process for an agrichemical is five to seven years from the time the patent is granted. Thus, agricultural chemicals are realizing far less patent protection than Congress originally intended.

In addition, passage of S. 1093 would accomplish four other important objectives:

1. It would sustain the incentive needed for agricultural chemical companies to continue to invest long-term, high-risk capital in research and development.

2. The bill would help to reverse the current trend of fewer and fewer new and improved agrichemicals reaching the marketplace due to the increasing time from discovery to commercial use.

3. The measure would help assure the availability of safer new agrichemicals indispensable for the doubling of food production by the year 2030 to feed a world population estimated to grow to 8 billion.

4. The legislation would enable U. S. agricultural chemical producers to maintain their leadership position internationally.

Conversely, failure to enact S. 1093 would be a decided negative for this industry and American agriculture. As members of this Committee and indeed the Congress know full well, the Nation's farmers are in perhaps the most dire straits since the Depression. Some fear that the actual condition of American agriculture may be even worse.

Agrichemicals enable the farmer to produce efficiently and with minimum risks from insects, weeds and diseases. Newer and better products will make him an even more effective food producer. But the innovation that is required to fulfill that need cannot come from an industry whose incentives are less than other segments of American industry. Only through aggressive and expensive, time-consuming research can the necessary, imaginative breakthroughs be made.

During the last 40 years, there has been significant progress in agricultural technology. Crop protection chemicals have revolutionized production techniques. Pre-emergence herbicides save American farmers more than $5 billion annually. Crop yields and quality have improved dramatically, providing adequate supplies of human food and animal feeds.

However, the past several years have seen the development of a potentially serious deterrent to the kind of progress expected of and needed in agricultural science. We have witnessed an ever-increasing time requirement for product testing to ensure that there will be no unreasonable toxic effects from these compounds on either human health or the environment. The agricultural chemicals industry totally agrees with these objectives. We want the day to come when no questions or fears will be raised about the use of our products. And our companies, with their great scientific bases, are working hard to make that happen.

But the evaluation of the data we must furnish has led to longer regulatory review periods. While careful reviews and testing requirements are necessary, they impose a significant and unwarranted penalty on the agrichemical industry. It is the decided shortening of the effective patent life for pesticides. As I noted earlier, on the average, five to seven years of a patent's life are consumed by these testing and regulatory processes, a diminution neither contemplated nor intended when the patent system was adopted in the early days of this Republic.

If it were not for the patent system, there would be fewer financial risks taken in an industry which requires substantial economic risk under the best of circumstances. Without the patent system, there simply would be fewer new developments in agricultural technology by private industry.

The financial uncertainties can be illustrated in several ways. For example, only one in about 12,000 chemicals tested by a company will possess the unique ability to selectively control a pest or disease with the necessary margin of safety. The cost of this process of identifying and screening these chemicals is significant. On the average, it now takes up to $40 million to bring a new product from discovery to market. If a new manufacturing facility is required -- and more often than not it is -- an additional expenditure of $40 - $70 million may be necessary.

When expenditures of this magnitude are coupled with a six-year erosion in the life of the patent, it becomes difficult to achieve a suitable financial return on these investments. Within the past six years, for example, one major pesticide company terminated four research and development efforts, in part because of insufficient patent life. The company eventually shelved miticide and aphicide candidates after difficult development left them with insufficient patent life to justify further expense. This action may become more frequent in the future as R&D costs rise and effective patent life becomes shorter because of regulatory requirements.

Before closing, I wish to mention why this legislation is again before the Senate after having been passed in the previous session. Last year certain interest groups opposed this legislation in order to achieve legislative changes to the Federal pesticide law, commonly known as FIFRA. We are currently negotiating with these groups, in a coalition of environmental, consumer, health and labor organizations, to respond to their concerns in amending FIFRA.

In summary, Mr. Chairman, without adequate patent protection, our member companies will be less able to undertake the increasingly costly and time-consuming research involved in discovering and developing new agricultural chemical technology which has heretofore led the world. This technology, combined with the ingenuity and efforts of the American farmer, have made this country the most productive agricultural nation in the history of the world. Enactment of S. 1093 will help us maintain this leadership.

ADDITIONAL COMMENTS OF JACK D. EARLY

PRESIDENT, NATIONAL AGRICULTURAL CHEMICAL ASSOCIATION

October 9, 1985

NACA wishes to go on record in regard to issues raised in opposition to Senate Bill 1093 at the hearing on September 10.

Most of the issues raised relate to operational and financial aspects of the agricultural chemicals industry. There were numerous questions and comments which referred to inflation, prices, industry profits and the like. Other comments called for an in-depth economic, agricultural and environmental analysis of the proposed legislation.

NACA wishes to state that these arguments are defective on two grounds:

First, the sole matter at issue and which Senate Bill 1093 seeks to rectify is loss of patent term due to regulatory requirements imposed by the Federal Government. The evidence is clear: the agricultural chemicals industry does not receive the full patent term of 17 years provided by law. As Chairman Mathias noted in his opening statement:

"The innovative chemicals for protecting food crops should have the same patent life as other products...one homely example would be floor wax. And the same principle of equity applies to the other chemical products addressed by Senate Bill 1093 -- the veterinary medicines that preserve the health of farm animals and domestic pets."

Senator Metzenbaum as well acknowledged this principle in a colloquy with Dr. Jack D. Early, NACA President. Senator Metzenbaum said:

"But I think the best argument you make, and I think it is a fair one, Mr. Early, is that, well, is it not a matter of equity that you have taken this time out of us by new regulatory procedures that did not exist 17 years ago..."

The Patent Law makes no provision whatever for other than evenhanded treatment for all patent holders. The law does not say that all patent holders are to receive 17 years of patent protection except for those in the agricultural chemicals and animal drug industries. Yet our industries clearly are accorded precisely such treatment. The reason is Federal regulatory requirements which consume five to seven years of our products' patent term, a development unforeseen when the Patent Law was enacted almost 200 years ago. Senate Bill 1093 seeks to redress that diminution of patent life, although even the bill does not provide in every case for full restoration of the patent term.

Second, if the arguments raised at the hearing are to form the basis for a decision not to provide patent term restoration for the agricultural chemicals and animal drug industries, then the same principles must be applied to all U.S. patent holders. Logic and consistency, therefore, would require that all patents presently in effect be reviewed on the same grounds, and adjustments in the length of those patents made in accordance with the factors that shorten patent life for the agricultural industries. Furthermore, all pending and future patent applications also must be reviewed on the same bases.

In sum, the arguments raised in opposition to Senate Bill 1093, in effect, propose that the Patent Law apply equally to all patents except those held by the agricultural chemicals and animal drug industries.

In the NACA presentation of its views on this bill, we stressed that equity is the central issue. Because there is not general comprehension of the particulars of this industry, we elaborated on adverse impacts the shortening of patent life has had and likely will have on the farmer, the consumer, and the national interest. These are the considerations that impel us to seek legislative relief. But even absent these factors, the merit of the basic argument remains undiminished: the agricultural chemicals industry does not receive the full 17 years of patent term provided by the Patent Law due to other requirements of the Federal Government imposed outside of the Patent Law. This industry does not receive the full 17 years of patent term enjoyed by non-regulated industries and enterprises.

We would like to address two of the issues raised during the course of the hearing.

Several assertions were made to the effect that enactment of Senate Bill 1093 would stifle competition in the agricultural chemicals market. When examined closely, it is clear that this is not the case.

If an agrichemicals manufacturer knows that it will be able to generate more profit on each additional product it develops, it follows that the company will seek to develop as many new agrichemicals as possible. More new products, then, will mean more profits for the producer. Therefore, it is logical to assume that the firm will attempt to develop as many new products as it can, thereby generating additional profits.

Other companies obviously will reach the same conclusion and take the same steps. Therefore, by increasing the profit incentive for manufacturing and marketing new products, Senate Bill 1093 will contribute to the development of more new products and thereby increase competition.

It is also important to recognize that within this process, the producer is not free to arbitrarily charge whatever price it wishes. The price for the new product must be attractive to the farmer. And the product must result in a net increase in efficiency and profit for the farmer. Otherwise, the farmer will not buy the product.

If the price of the new agrichemical does not impact the farmer's bottom line positively, then he will continue to use an older product already on the market or another new product which increases his profit and efficiency.

Thus, the price of an agricultural chemical is not dictated by the manufacturer but by the market.

Another question raised during the hearing was why five selected agrichemicals were sold at a lower price outside the U.S. than inside. The implication was that the products were marketed at higher prices within the U.S. because they were under the protection of the U.S. Patent Law. A few points warrant mention in this regard.

All five of the products cited -- Carbaryl Technical, Methyl Parathion Technical, Paraquat, Maneb, and Toxaphene -- are all off patent, i.e., their patents have expired. Therefore, the price differential has no relationship whatever to U.S. patent protection and cannot be attributed to it.

There are many reasons why an agrichemical may be sold at a higher price domestically than abroad. Some products have duties levied on them when imported. For example, the duty on U.S. imports of Parathion is currently 13.8 percent. In other cases, currency fluctuations may cause price differentials. In still others, it may be cheaper to manufacture an agricultural chemical abroad than it is in the U.S. For example, Paraquat is made in Taiwan by 8 to 12 producers. Labor costs in Taiwan are considerably less than in the U.S.. Moreover, the Taiwanese plants that produce Paraquat are not required to conform to U.S.

health and safety standards for similar plants. Therefore, the cost of production is much less in Taiwan than in the U.S.

In many cases, an agrichemical will sell at a higher price outside the U.S. than within. For example, a wheat herbicide under patent in the U.S. and marketed in the U.S. and abroad sells for over 20 percent more in Europe and elsewhere than in the U.S. There are several fungicides under patent in the U.S. which sell for more in Asia than in the U.S. A corn herbicide sells for more in South Africa than in the U.S. A grass crop herbicide sells for 50 percent more in Latin American countries than in the U.S. Therefore, there is no basis in fact to contend that U.S. patent laws cause agricultural chemicals sold in the U.S. to cost more than they do abroad.

From this, it is obvious that there is no uniform pattern of pricing differences between the U.S. and foreign countries. In some cases, products are sold at higher prices domestically, for any number of reasons, and in other cases, products are sold for less in the U.S.

Senator **Mathias**. Senator Metzenbaum, do you have any questions? You have some dirt farmers here now who could talk to you from a farmer's point of view.

Senator **Metzenbaum**. Well, I am impressed by the testimony of Mr. Cawley, Mr. Holloway, and Dr. Early. Let me see if I understand it correctly.

If we pass this legislation which will permit up to 5 years patent extension, then we are going to get more research and development, we are going to reverse the trend of a lesser number of new chemical products coming to market, and we are going to assure our continued leadership in the international marketplace.

If we do that in 5 years, why do not we do it permanently? Why are we not here considering a bill just to make the patents permanent, gentlemen? If there is merit to your position, then you ought to be in here telling us that the patent ought to be a permanent one. Why not that?

Mr. **Cawley**. I will try to answer in my own farmer way that I think the bill is to give them that extra 5 years so they can get their costs back for a chemical and so the rest of the chemical companies would come on. But once you find a good chemical that is not harmful to the environment and harmful to the human race, then it is open to anybody to go ahead and produce it. And I think that is the part there; let the world produce it if it is a good chemical and it works.

Senator **Metzenbaum**. Not if you have a patent on it. Everybody cannot produce it if there is a patent on it. That is what this whole bill is about.

Mr. **Cawley**. They can after a certain length of time.

Senator **Metzenbaum**. Sure. But you are saying that you need an extension. Chemical companies are not claiming poverty. Nobody is in here saying the chemical industry is on its last legs or that they somehow need some help from their Government in order to bail them out. I have not looked at the financial reports of chemical companies, but that is my understanding. And if you care to comment on it, Mr. Early.

Dr. **Early**. I would like to comment, Senator, if I may.

Senator **Metzenbaum**. Let me just point out here, I have one article my staff has just handed me saying that agricultural rebound enriches chemical earnings. A big rebound in demand this year for major agricultural chemicals including fertilizers and pesticides provided substantial added momentum to the general upsurge in the chemical industry's second quarter sales and earnings.

It is only fair to point out to you that is August 3, 1984. It is not 1985, but go ahead, if you care to.

Dr. **Early**. I will be glad to come back to that last article you just quoted and could cite to you some companies that would not agree with that. But let me go back to your earlier question

I think we are looking at a matter of equity here, and your question, would you like to have a monopoly on your invention forever, the answer to that is yes, surely. Any inventor who invents a product would like to have the right to have a monopoly on his product forever and ever. You would like that and I would like that if I came up with some innovation.

But what we said back in 1790—back in 1790—is that a 17-year period of time is the right period of time for someone to recoup their investment or to get some return on their invention. And so the Congress recognized that and we recognize it.

What we are talking about here is an inequitable situation. We are not getting the 17 years that everyone else is getting. We are not asking for any more or any less. We are asking to come up with 17 years. Now, is that not fair?

Senator **Metzenbaum**. Let me ask you a question.

Dr. **Early**. Yes, sir.

Senator **Metzenbaum**. When a patent runs out, maybe the 17 years is too long in the first instance. Maybe it should have been 12 years or 15 years or maybe it should have been 22 years. I do not know. But we have lived with it a long time.

Now, is it not a fact that when a patent runs out, prices normally go down?

Dr. **Early**. I think that is true. Prices will likely go down for that particular product. But I think that the Senator is missing the basic point here. What we are talking about is a farmer buying a piece of technology to grow his crop, that he is investing x dollars. And unless that farmer, who is certainly a very sharp businessman, is getting a return of $1, $2, $3, $4, $5 on that investment, he is not going to buy that product. I do not care whether it is on a patent or whether it is not on a patent. It is a matter of economics.

If I am out there farming growing corn and I want to control the weeds in my corn out there, I am willing to invest a dollar to do that, for example, but I better get a significant return on that investment or I am not going to buy it.

Senator **Metzenbaum**. I think the difficulty, Mr. Early, in your argument is that, A, the premise is that if you have a longer period, you are going to invest more in research and you are going to therefore produce more products and therefore the farmer is going to be helped that much more.

The contrary position has to be what proof is there that that is the fact. Right now, chemical companies are busting their butt trying to find new products for the very simple reason we are in a free enterprise system in order to make a profit. And what concerns me is that when we extended the drug patent laws, which I claim that we should not have done and which I voted against, all we did is assure the drug companies that they would have an opportunity to charge higher prices for a longer period of time.

Now, I believe that the farmers, and I am frank to say this to you, Mr. Cawley and Mr. Holloway, I think that you have been sold a bill of goods, because I do not think that there is any evidence that you are going to get more products. Certainly there is no evidence that you are going to pay less money. The contrary is the fact. You are going to pay more money if the patent is extended. And I understand how somebody could make that argument to you, but my simple economic theory, and it is not a very complicated one, and that is that where there is competition, prices are going to go down. And Mr. Early, I think, is very candid in saying that is correct. When you have competition, when the patent runs out, the prices will go down.

Now, that then leads me to the point of saying, well, why are we asked to do this? Farmers are here, the secretary of agriculture of Maryland, and the Farm Bureau is here, saying that we think this is good for the farmer. If I thought it was good for the farmer, I would be for the bill. If I thought it was good for the American consumer, I would be for the bill. But I think the best argument you make, and I think it is a fair one, Mr. Early, is that, well, is it not a matter of equity that you have taken this time out of us by new regulatory procedures that did not exist 17 years ago, although I would guess that there were some that existed at that time.

Dr. Early. Minimal, though, Senator. Minimal.

Senator Metzenbaum. I do not know what the fact is and I will have my staff check to find out what regulatory delays occurred in the past, not necessarily when the law was passed. When was it passed originally? The 17-year requirement?

Dr. Early. 1790, the patent.

Senator Mathias. That was the original patent law, but of course, the concept was embodied several years earlier in the Constitution, which provided authorization for it.

Senator Metzenbaum. Well, I think the real question is, is there enough equity to merit passage of this bill notwithstanding the fact that it will cost the American farmer and the American consumer additional dollars. I am not at all convinced that there is any merit to the argument that it will produce more research, more products, that it will help maintain our leadership in the world. I do not think any of those things follow as a matter of course. But I am not here to debate it. You have other witnesses, Mr. Chairman, and I will give back the floor.

STATEMENT OF VAUGHN D. BRYSON

Mr. Bryson. Can I just add one comment, please, Senator. I think that——

Senator Metzenbaum. Would you please identify yourself?

Mr. Bryson [continuing]. I am sorry. I am Vaughn Bryson. I work for Elanco, a company that markets both agricultural chemicals and animal products.

Senator Metzenbaum. I will let you make any comments you want if you let me ask some questions about how come Eli Lilly did not have a tougher time with the Justice Department. But that is out of your department. You are not in on that. Go ahead.

Mr. Bryson. The implication is that patents create a monopolistic situation. I would just like to speak from my own personal experience. Our perception is that patents do not eliminate competition. Let me give you a specific example. We have the leading grass herbicide sold in the cotton market and the leading grass herbicide sold in the soybean market. But there are five other compounds that have been marketed in the same chemical class, even though we had patent protection.

The selling price on our product today is now less than it was when it was introduced in 1964, even though we had patent protection during that period of time. And I think——

Senator **Metzenbaum**. But is that not because somebody else was able to make a product similar enough and not violate the patent law to be competitive with your product?

Mr. **Bryson** [continuing]. Exactly. But it is still a highly competitive market even though we were patent protected.

Senator **Metzenbaum**. If you had a patent that was so solid, so tight that nobody could take off on it, then you would not have that kind of competition. I think, for example, the one we all think about these days is aspartame, where the patent appears to be so tight that there is no competition to manufacture aspartame.

Mr. **Bryson**. But we are back to the free enterprise system again. Now that aspartame has become a big product—my prediction is in the next 5 to 10 years you will see a significant number of sweeteners that, if they get through the regulatory process, and there are several are in the pipeline—you will see significant competition in the sweetener market.

And that is exactly what we have seen in the United States in the agricultural chemical market, regardless of which segment you look at.

Senator **Metzenbaum**. I guess on that basis that you really saying a patent does not make any difference so why should we extend it?

Mr. **Bryson**. I do not think that is true at all. What patents really do is provide the incentive for companies to invest. The thing that has changed in the last 10 or 15 years is that the investment required to develop a new compound has gotten to be so significant, especially with the time required to get a new product to market. In all honesty, I do not think the agricultural chemical industry today or the animal products industry today is getting an acceptable return on their research and development investment.

Senator **Mathias**. What is the time required in an average kind of situation to recover the capital that is invested in research and development and promotion, all of the leading factors that go into putting a drug on the market?

Mr. **Bryson**. Well, that is a tough question. It obviously depends on the magnitude of the product and the investment required.

Senator **Mathias**. When I said average, I do not suppose that there is any average that is definitive, but what would your guess be?

Mr. **Bryson**. I find that impossible to answer.

Dr. **Early**. Let me guess on an average basis; obviously it is going to be different.

We are looking at something in the neighborhood of 6 to 8 years from discovery until we put a product on the marketplace for sale. And when you say, well, how long before you get a return on the investment of $40 or $50 or $60 million, that is hard to say because the marketplace dictates that.

As I said early on, you cannot go out and arbitrarily charge a price to the American farmer to buy your product. You could charge him, you know, $5 a gallon or $10 or $30 or $40 a gallon, provided the American farmer is going to get a return on that investment. But only to the extent he is going to get a significant return on investment.

So we just cannot look at what it costs us and then try to prorate it out over *x* number of years and say this is what we are going to charge, because we got competition out there, and it induces the farmer to pay for what he thinks he is going to get a return on the investment.

I do not really think there is an answer to your question specifically, except that the delay period is something like 8 years, and it may cost, you know, $40 or $50 or $60 million to put it there.

Senator **Mathias**. Looking at this bill as against the human pharmaceutical bill we had before us last year, what is the impact of the difference in this kind of situation? When you deal with human pharmaceuticals, by and large you are dealing with products that a doctor tells a patient to take. The patient does not have a lot to say about it. The doctor gives the patient the prescription and the patient takes it to the drugstore and it gets filled.

In agrichemicals you are dealing with a different kind of a factual background. The farmer, by and large, has to make up his own mind whether he wants to buy the chemical. He has to figure out that it is going to be to his advantage to make this purchase and that he is going to recover that investment in terms of higher yields, better quality.

How does that impact on the different patent situations?

Mr. **Bryson**. There are several differences between the pharmaceutical industry and the agricultural industry, and you have hit on the important one. When a physician makes a product selection decision, he is making an intuitive, cost-benefit choice for that patient. When the farmer makes that decision, like Mr. Cawley, he is making his own cost-benefit analysis. He is looking for a specific return and in many cases that is easily quantifiable for him, quantifiable in terms of yield or in the animal industry increasing meat production or controlling disease.

However, there are a couple of major distinctions. You are talking about relatively small industries with the animal products and agrichemicals compared to pharmaceuticals. On a worldwide basis, animal products is one-twelfth the size of pharmaceuticals; ag-chem is about one-sixth the size. On the other hand, the research and development costs for a new product average only slightly less than half the cost of a new pharmaceutical. And consequently, the cost of new product development is much, much higher in relation to potential.

When you combine that factor with the fact that our customers are evaluating the economic return when they purchase an animal product or an ag-chem product, you have got a very, very different economic situation.

And that is the exact reason we had the support last year when this bill was introduced of 33 farm organizations around the country, and this year we should have a similar base of support for agricultural patent term restoration.

Senator **Mathias**. Senator Metzenbaum?

Senator **Metzenbaum**. Let me ask you if these are all agricultural chemicals: Carbaryl technical, methyl parathion tech., paraquat, maneb, toxaphene?

Dr. **Early**. Yes.

Senator **Metzenbaum**. Would you be good enough to explain to me why it is, and this is a couple years old, but when the U.S. price for carbaryl technical was $2.35 a pound, the foreign price was $1.80. When the U.S. price was for methyl parathion technical was $1.35 a pound, it was being sold overseas for $0.92 a pound. And the first one was a Union Carbide product; the second one a Monsanto Chemical product. Chevron was selling paraquat for $33 a gallon in the United States and $10.20 a gallon in Taiwan and various other places.

Rohm & Haas and DuPont were selling maneb at $1.40 a pound in the United States, $1 per pound in Europe. And BFC Chemicals, Inc., was selling toxaphene at $0.67 a pound in the United States and $0.41 to $0.43 a pound in Brazil. And there are many more commodity products that fall into that category of Ciba-Geigy, Dow Chemical, FMC Corp., Stauffer Chemical, Bayer, and Shell Chemical.

How do you explain the fact that the American farmer has to pay more for products manufactured in this country for the protection of U.S. patent laws than the farmers have to pay overseas?

Dr. **Early**. First of all, I am not privy to why these pricing situations took place and how they took place, so whether they are still valid today—this is a couple of years old—I just do not know the answer to that.

But I think what you have to look at——

Senator **Metzenbaum**. Let me tell you. I am reading from a letter addressed to the FTC from the Drexel Chemical Co., addressed to Mr. William C. Holmes, attorney, Chicago regional office of the Federal Trade Commission, dated May 17, 1982, and signed by Robert D. Shockey, president of Drexel Chemical.

Dr. **Early** [continuing]. Yes. I know the gentleman. I do not really have the obvious answer to why prices may vary from country to country, or in this country or some other place. I do not know what the mechanism was for setting up those prices. And I am not privileged to that.

I think we go back to the fact that what I was talking about here early on was the return on the investment in this country. And you are talking about commodity prices, commodity items out there where the prices are going to go down. Some of the newer products coming on, Senator, may be doing the same job out there controlling the grasses and the weeds, you know, much more efficiently than the other products are controlling them out there.

So I just do not have a good answer for you in that area.

Senator **Metzenbaum**. Let me ask you another question. One of the arguments that has been persuasive in bringing on the farm groups is that if you get the patent law extension you will be able to spend more money on R&D. Were the farm groups aware of the fact that back in 1975 chemical companies were spending 6½ percent of their total sales on R&D; by 1980 they were up to 8½ percent of their total sales on R&D; by 1983 they were up to 11.9 percent, almost double what it was in 1975, on R&D. And it seems to me, Mr. Early, that the evidence is very convincing that even with the present law that the expenditures on R&D are increasing substantially, very substantially, and that the profits of the chemical companies are holding up. There may be a down trend somewhere along the line, but I think over a long period of time they have done well. And under those circumstances why should the American farmer be persuaded that this is in their best interest, or his or her best interest? And that is the thing that I do not understand, because we are getting more investment, making more profit, they will have to pay more. We already agreed to that. I do not understand why these men are here so enthusiastically supporting it. You have done a great sales job.

Dr. **Early**. They are going to pay more, but if they pay more, if they are getting instead of a $3 return on their dollar they are getting $6, it makes sense then, does it not?

Senator **Metzenbaum**. Well, of course, but there is no indication that extending the patent is going to give them $6 instead of $3, because you are already trying to bring the best products to the market that you can so that you can, in turn, sell them to the American farmer.

Senator **Mathias**. Please, Senator Metzenbaum, restoring the patent.

Senator **Metzenbaum**. Restoring a patent.

Dr. **Early**. Thank you, Mr. Chairman. [Laughter.]

I think it really goes back, because no matter how, you know, how much you have invested or what you have done, you have got to compete with the existing products on the market. And I think you ought to recognize, Senator, that as I was sitting here, I cannot really think of any pest that is a pest in agriculture today, and maybe friends in the farm community can speak to this, where we do not have more than one product that we can eliminate or control that pest. So there is a lot of competition existing out there. The new products coming on hopefully are going to be more efficient, more effective, safer for the environment we hope, and that is an incentive, I think, for the farmer to use that product, to get a greater return on the investment, safer for the environment, safer for the user and the applicator.

Senator **Mathias**. I would like to have a couple of alternatives on groundhogs.

Mr. **Early**. Senator, I would like to have one too, yes. The market is not big enough, Mr. Chairman.

Senator **Metzenbaum**. The secretary of labor is here. I had a previous meeting with him. Would you please excuse me. No offense to the witnesses.

Senator **Mathias**. Thank you very much, Senator, for your participation.

Secretary Cawley, let me ask you and Mr. Holloway a little bit about the support of this concept in the working farm community. I think it was mentioned there were 33 farm organizations that were in favor of this legislation, certainly an impressive number of farm groups. How widely do you think the bill is understood by the farm community?

Mr. **Holloway**. Senator, I think the thing that agriculture understands the most is the fact that since the passage of the 1972 amendments to FIFRA, we have lost better than 50 percent of the agricultural chemicals by volume that we use. I think that one of the answers to Senator Metzenbaum's question about the increase in the R&D funds, yes, they have to, or we will simply be out of business, we will back to the horse and buggy days.

I do not think any consumer in this country wants that. The other statement that the Senator made that I take issue with is the fact that he said it would cost consumers more. I have never seen anything in agriculture in this country that increased efficiency that was not passed totally to the consumer. The consumer in this country has a cheaper, safer supply of food today in terms of expendable income than they have ever had in the history of this Nation, and that is what we are trying to protect.

I think the people in the field are aware of the losses of these chemicals; they are also aware that any company, any business has to look at the bottom line. And if they cannot recoup their costs of research and development, production, then there simply will not be chemicals, environmentally safer chemicals to replace those that we are now losing.

Mr. CAWLEY. Mr. Chairman, may I add to that?

Senator MATHIAS. I wish you would.

Mr. CAWLEY. As a farmer, what disturbs me, if you go back in agriculture and check our history, we are not using the chemicals we used 10 years ago. We are not using the chemicals we used 20 years ago. Some of them have been improved; others have just lost out because of immunity. And in any business, look at our machinery, look at this efficient agriculture. We have had to keep one step ahead of whatever is in front of us. And the chemical companies have done this with their chemicals.

I cannot, on a farm, I do not give a darn who produces it or where it comes from, two things: Will it do the job and can, my bottom line, show some more profit? I really depend on the EPA to tell me whether it is a good chemical or bad chemical. They already automatically tell me I can use it or I cannot use it, whether it is a restricted chemical or a free-flowing one we can use.

So it just bothers me that as the competition gets higher and the demands—I can understand why the research funds went up; they have to go through so many more steps to prove to the EPA that this is not going to harm the environment, not going to harm the people. And they are spending more money on each chemical. Therefore, they need this time to recoup some of that money that is spent on this research and development. The American farmer will use those chemicals that, No. 1, do the job and that the cost is reasonable. And I do not care how great the chemical is, if the price is not in the ballpark, he will not use it.

So the patent law has to be favorable to all so that we get our fair share of the proper chemicals we use, just like a human being does. We must have these chemicals to survive. We are in a hell of a shape now. We are not making a profit. And we are using chemicals now that we are only using 1 ounce per acre, and that is research and development—and it saves machine time across the field—and they must recoup that. And I insist that, contrary to what the Senator is saying, that we do not know what we are doing because chemical companies are making huge profits and selling the chemicals someplace else. But I know that around the country, around the world, that we are not allowed to use chemicals or some of the chemicals that are used in other countries in this world, and those products are shipped in here.

Our chemical companies are under the gun in this country, more so than those food products produced outside this country and allowed to come into this country. They are under the gun; we need this so we can continue to stay in business.

Senator Mathias. And it is your opinion, I take it, the farm community that you speak for and represent, thoroughly understands the economics of this issue.

Mr. Holloway. Senator, this is not a new issue. We have been discussing this now, what, 3, 4, 5 years, I guess, at least. So it is not a new issue.

Mr. Cawley. And when 17 members of a 17-member agricultural advisory committee to the secretary of agriculture of the State of Maryland says we want this for agriculture, I think they know what they are talking about.

Senator Mathias. That is what I want the record to reflect very clearly, because I think the Senator from Ohio has raised some serious questions and I think the record ought to satisfy them.

I want to thank you all for being with us this morning.

Our third panel will be Mr. Jack Doyle, director of agricultural resources, Environmental Policy Institute, and William Haddad, president of the Generic Pharmaceutical Industry Association, a familiar face in this room.

Gentlemen, we will ask you to observe the 5-minute rule in your initial presentations, and full statements will, of course, be included in the record.

STATEMENT OF A PANEL, CONSISTING OF JACK DOYLE, DIRECTOR OF AGRICULTURAL RESOURCES, ENVIRONMENTAL POLICY INSTITUTE, WASHINGTON, DC; AND WILLIAM F. HADDAD, PRESIDENT, GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION, NEW YORK, NY

Mr. Doyle. Mr. Chairman, I have a full statement here that I have distributed to the committee, and I would ask that it be included in the record.

Mr. Chairman, I am Jack Doyle of the Environmental Policy Institute, a nonprofit, public-interest organization engaged in research and public education on environmental and natural resource issues generally. We thank the committee for the opportunity to appear here today.

We think this is a very important issue, and we think these hearings, in fact, are very important—one of the first times that a broad cross section of organizations has been asked to testify. In all due respect to some of the former witnesses, we think that it would be very important to have farmers come in and give their perspective in this legislation in person; and I, for one, would be helpful in providing names of some farmers that I have been in contact with that have some concerns about this legislation.

Although we are fully aware that the patent term extension law has been approved by Congress for human pharmaceuticals, we believe that this legislation for agricultural products has not been subject to the same level of debate and data gathering on industry trends, innovation rates, pricing impacts and other questions. For this reason, we feel that the proposed legislation should not move beyond this subcommittee until there has been a real thorough investigation and study of some of the questions to determine whether, in fact, the legislation is needed.

Therefore, we recommend that this subcommittee and/or full committee authorize an appropriate congressional investigation or other Government agency study into a number of important areas. We have listed some of these in our testimony [see prepared statement]. I will try to summarize this list briefly for you. We think, for example, that some of the questions that should be investigated include the rate of product innovation in pesticide and animal health products—has the rate of innovation really declined? I think, judging from the former panel of witnesses, that there are not real clear answers to any of those questions, several of which were raised by yourself and Senator Metzenbaum.

We have one report from Chemical Week, for example, that points to 22 new herbicides, slated for product registration during the 1985-90 period. We think that is an indication of some measure of innovation in agriculture under the present system.

Second, when are research costs recouped? I think that question was asked of the former panel, and I think there were some indications of confusion in the answers to that question. I think that is another indication that we need some hard data to resolve those kind of questions.

EPI would like to see more information compiled on profitability profiles of the companies involved in this business over time. The agriculture sector is one that is fluctuating and is cyclical in nature, and that has to be taken into account when you examine profitability trends in the industry.

Another area that we feel is particularly important are the economic concentration ratios of manufacturers in particular pesticide and animal health markets and submarkets, such as the corn and soybean herbicide submarket, for example, and the submarket ratios for particular livestock health products, be they antibiotics or medicated feed ingredients. When you look at these particular submarkets, and the particular rates of concentration in those markets, what is the rate of innovation within those submarkets? And again, what are they over time?

A very important question to us is No. 6 [see prepared statement] in our list of areas we feel need to be looked into. To what extent do patents generally, and patent term extension specifically, if it is enacted, contribute to product lifetimes and an economic entrenchment of products that may be dangerous to the public health or safety. Once patented, for example, is it more difficult to effectively regulate and, if necessary, recall a dangerous product from the marketplace? We think that is a very important question that needs to be answered.

Another concern of ours has to do with innovation in the area of agricultural alternatives. We believe that biological alternatives—even innovative, on-farm practices, such as crop rotations, offer alternative practices that farmers can use to save money while protecting the environment. What are the innovation rates in those and other biological product areas and how have they been affected by patents in the chemical and animal health area? We think that is an important question that needs to be answered. Is there, in fact, a stifling of research into biological alternatives because of the economic weight of conventional products already under patent. We think that issue is one that needs to be addressed in detail.

The question of pricing differentials among agricultural pesticides and livestock drugs in this country and other countries overseas was already raised by Senator Metzenbaum, and it is included in our list as well. It is also important to include how such differentials may affect rates of return here and, again, profitability and the need for patent-term extension.

In No. 9 in our list, we have indicated some concern about the coincidence of the expiration of patents on some very popular products in the last several years, with the move to come on strong with patent-term extension in those agricultural product areas. We think that is something that should also be looked into.

Another question relating to the pending FIFRA bill—and here I might correct the record. I believe it was Mr. Early from the National Agricultural Chemicals Association who mentioned the ongoing negotiations with the environmental community vis-a-vis FIFRA. EPI is not a signatory to that process or any agreement which would appear to trade our concerns about this bill, and I believe there are also other environmental groups who are not in total agreement with those negotiations.

But in regard to FIFRA, there are provisions in the existing pesticide law that we believe have patent-like application and some exclusive use provisions, and wonder how these FIFRA provisions would offset those in the existing patent law. And again, in the list of things that we think should be thoroughly looked at before this legislation moves, is that relationship. If this patent extension legislation is adopted coupled with those exclusive use provisos in FIFRA, what effect will they have on product lifetime, profitability, and product innovation?

Finally, we think a real important question would be to look at other ways that agricultural innovation might be stimulated, either through the Tax Code, through public research, or certain kinds of investment incentives to help entrepreneurial innovation in agriculture. We think that those alternatives should be looked at as a way to spur product innovation in agriculture, and not just simply look at patent term extension as the only way to move new innovation forward in the agricultural area.

In summary, Mr. Chairman, these are only some of the questions we believe deserve answering in an indepth economic, agricultural, and environmental analysis of the proposed legislation. We believe that exploring and addressing these and other issues will serve the best interests of farmers, consumers, and the public at large.

We appreciate the opportunity to appear here today to express our views, and we will gladly work with the subcommittee in outlining the details of our recommended study.

Thank you.

Senator MATHIAS. We appreciate that, and we let the time run over a little bit, because you had serious questions to propose to the committee.

Mr. **DOYLE**. I might add, Mr. Chairman, one other point. We too are concerned about the Chesapeake Bay, and we have a full-time staff person working on the Chesapeake Bay year round.

Senator **MATHIAS**. We are very grateful for that assistance. We need all the help we can get.

[Statement of Mr. Doyle and additional submissions for the record follow:]

PREPARED STATEMENT OF JACK DOYLE

Mr. Chairman, Members of the Subcommittee:

My name is Jack Doyle, I am Director of the Agricultural Resources Project for the Environmental Policy Institute (EPI). EPI is a non-profit, public interest organization engaged in research, public education, litigation and lobbying. Our researchers and lobbyists work on energy, environmental and natural resource policy at the local, national, and international levels. We appreciate the opportunity to appear before this subcommittee today to share our views on the topic of agricultural patent reform.

Mr. Chairman, EPI's position on S. 1093, or any similar bill, is that such legislation should not move beyond this subcommittee at this time. Although we are fully aware that a patent term extension law has been approved by Congress for human pharmaceuticals, we believe that this legislation for agricultural products has not been subject to the same level of debate and data gathering on industry trends, innovation rates, pricing impacts and other questions. Further, given the dire economic circumstances now confronting our nation's farmers, we think it fully advisable for this committee to be especially attentive to the cost-of-production impact that this or any patent-term extension bill could impose on farmers and ranchers in the future.

Therefore, we recommend that this subcommittee and/or full committee authorize an appropriate congressional investigation or other government study into a number of important areas to determine whether this legislation is needed, and what its impact will ultimately be on agriculture, farmer and consumer pricing, and the environment. For example, among the questions that need to be answered are the following:

1) Are there unbiased economic data which show that product innovation in pesticide and animal health products has declined in the last 5 to 10 years? There is at least one report from Chemical Week that notes some 22 new herbicides slated for registration in the 1985-1990 period.

2) How soon after the discovery and "market launch" of new pesticides and animal drugs are research costs recouped? And how are "research costs" calculated by manufacturers?

3) What has been the pesticide and animal drug industries' profitability profile, plotted historically, over longer and shorter periods of time, examining periods of high and low innovation, and selecting for R & D investments made during periods of popular pesticide and animal health products?

4) What are the economic concentration ratios of manufacturers in particular pesticide and animal health markets and submarkets, such as corn and soybean herbicides or particular kinds of livestock pesticides, such as animal growth hormones, antibiotics, and medicated feed ingredients?

5) In highly concentrated submarkets, what has been the rate of innovation and new product introduction?

6) To what extent do patents generally, and patent term extension, contribute to the product lifetime and economic entrenchment of products that may be dangerous to the public health & safety and protection of the environment? Once patented, is it more difficult to effectively regulate and if necessary, recall dangerous products from the marketplace?

7) Do patents on certain agricultural products such as pesticides, animal drugs, and now agricultural microbes with biotechnology, have an impact on the rate at which alternative agricultural products and practicies are introduced and adopted? Is there a stifling of research into biological alternatives and a lack of economic incentive in the marketplace because of the economic leverage and economic dominance that patents on conventional products confer on a few agricultural product developers?

8) Are there pricing differentials on agricultural pesticides, herbicides and livestock products between the United States and other countries? Allowing for all the variables and making adjustments for inflation factors and currency exchange, are one manufacturer's pesticides sold for much higher or lower prices in other countries than they are in the United States, and if so, how do such differentials affect return on investment rates at those companies?

9) What is the coincidence of patent-term expiration of important and popular pesticide and animal health products now on the market, and the recent move to secure patent-term extension for agircultural products of those same kind?

10) If this legislation is adopted, what will be the combined effect of these patent-term extension

provisions with certain patent-like and exclusive use provisions now found in federal pesticide laws?

11) What effect will enactment of this patent-term extension bill have on the pesticide regulatory process? Will it improve that process or make it more lackadaisical? In this regard, we belive it would be important to obtain the views of EPA pesticide officials in this suggested study as well as in subsequent hearings.

12) What other non-patent strategies and/or policies might be pursued by government and/or businesses that would spur agricultural product innovation in the private and public sector? Might some tax, investment, or public research strategies aimed at entrepreneurs be more or equally effective at stimulating product innovation, or innovative on-farm practices that could compete with particular product lives?

In summary, Mr. Chairman, these are only some of the questions we believe deserve answering in an in-depth economic, agricultural, and environmental analysis of the proposed legislation before this subcommittee. We believe that exploring and addressing these and other issues will serve the best interests of farmers, consumers and the public at large.

We appreciate the opportunity to appear here today to express our views, and we will gladly work with this subcommittee in outlining the details of our recommended study on the ramifications of agricultural patent reform.

ENVIRONMENTAL POLICY INSTITUTE

August 7, 1984

TO: Members, House Judiciary Committee

RE: H.R. 6034, The Agricultural Patent Reform Act of 1984

The Environmental Policy Institute strongly urges you to vote against full committee approval of H.R. 6034, the Agricultural Patent Reform Act of 1984, for the following reasons:

- The need for H.R. 6034 has not been substantiated. The chemical and pharmaceutical industries have not shown why patent term extension for pesticides and veterinary products is needed. They have not produced economic data which show that product innovation or return on investment is suffering under the present system. R&D in new pesticide and veterinary products has increased in recent years rather than decrease. In the herbicide area alone, at least 22 new products are slated for registration in the 1985-1990 period.

- Present regulatory system is not onerous. While testing and regulation of new pesticide products may consume some years of a product's exclusive marketing life, R&D costs for popular products are often recouped in one or two years, leaving 10 or more years of exclusive marketing. Moreover, experimental use permits from EPA add to a product's effective market life.

- Agrichemical profitability at all-time high. A number of companies -- including Monsanto, W. R. Grace, Uniroyal, DuPont and American Cyanamid -- have reported very substantial, and in some cases, record-breaking second-quarter earnings for 1984 because of agrichemical sales. Monsanto's CEO, Richard J. Mahoney, recently emphasized the important role that agricultural chemicals played in helping that company to the best second quarter earnings in its history. Uniroyal too, noted that its second quarter earnings for agricultural chemicals were the strongest ever. (see enclosed article, "Agricultural Rebound Enriches Chemical Earnings", *Journal of Commerce*, 3 August 1984).

- Pesticide reform and public health and safety set aside. H.R. 6034 provides an economic windfall to the agrichemical industry while Congress, for the last two years, has taken little action to protect the public's health and safety in the area of pesticide testing and regulation. Both FIFRA reform and food safety bills currently lag in Congress while H.R. 6034 is pushed ahead with unprecedented speed.

- Patent term extension for pesticides will discourage pest-management innovation. By giving longer patent terms for pesticides and veterinary products, Congress will be encouraging further capitalization of a research infrastructure geared to produce chemical-based agricultural products. Moreover, longer patent

(over)

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terms for such products mean longer product life, and consequently, less of an incentive to innovate beyond the bounds of familiar chemistry. Thus, longer patent life will help to bias research and capital investment in one direction. With such an incentive for pesticide production, commercial investment in alternative pest control strategies and products will be discouraged.

- H.R. 6034 may increase economic concentration in pesticide industry. In a 1981 FTC staff paper investigating 4 agricultural input industries, it was discovered that four-firm and eight-firm concentration ratios in the pesticide manufacturing industry were 57 percent and 79 percent respectively. Sub-market concentration, as in corn and soybean herbicides, as well as corn insecticides, was found to be substantially higher (see enclosed tables). The issue of potential anticompetitiveness in the pesticide industry has not been explored in the consideration of H.R. 6034, yet patent term extension in this area could figure prominantly in both farm costs and food prices.

- H.R. 6034 includes biotechnology patents prematurely. Regulation of commercial products and processes using biotechnology and gene-splicing technologies has not been addressed by Congress. Regulatory time frames for such products, therefore, are unknown at present. EPA, for example, has yet to issue even a discussion of principles in this new area of product regulation. Legislating patent-term extension for biotechnology products at this time, therefore, is premature.

- Biotechnology products pose new patent & environmental questions. In the area of agricultural biotechnology research, several major chemical and pharmaceutical companies are working on ways to move herbicide-resistant genes into crops such as corn, soybeans and wheat. How will these new products of agricultural biotechnology be patented? Will both the gene and crop variety be patented as one entity in this situation, or will they be patented as separate pieces of a product package? Moreover, will patent term extension for such products serve to increase the use of synthetic pesticides in the environment?

- H.R. 6034 provides patents for food-producing substances. Congress has not explored the economic and environmental ramifications of patenting powerful substances such as genes, plant growth regulators, microbial pesticides and livestock hormones that will account for the control and cost of agricultural productivity and food production.

In sum, the Environmental Policy Institute urges you to oppose this legislation at this time, as the issues of patenting, biotechnology, food production and environmental quality are increasingly intertwined, and worthy of more scrutiny and analysis than Congress can provide in hasty, end-of-the-session legislation.

Respectfully,

Jack Doyle, Director
Agricultural Resources Project

Enclosures

MARKET SHARES FOR SELECTED PESTICIDES

	Top 3-4 Firms	Combined Market	Year	Source
All Herbicides	Ciba Geigy Monsanto Stauffer Dow	71%	1976	USDA-ESCS
Corn Herbicides	Monsanto Ciba Geigy Stauffer Shell	87%	1978	USDA, FTC
Soybean Herbicides	Monsanto Eli Lilly BASF	63%	1980	USDA & 1981 Farm Chemicals Handbook
Grain Sorghum Herbicides	Ciba Geigy DOW Monsanto Shell	75%	1980	USDA & Chemicals Economics Handbook
Cotton Herbicides	Eli Lilly Ciba Geigy	52%	1979	USDA & 1981 Farm Chemicals Handbook
All Insecticides	Monsanto Hercules Stauffer FMC	46%	1976	USDA-ESCS
Grain Sorghum Insecticides	FMC Monsanto Union Carbide	62%	1980	USDA & 1981 Farm Chemicals Handbook
Corn Insecticides	Am. Cyanamid FMC Stauffer	78%	1980	USDA & 1981 Farm Chemicals Handbook

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Note: Data compiled by the Environmental Policy Institute, Washington, D.C.

WASHINGTON POST
1 AUGUST 1984

Pesticide Bill Change Mystifies Lawmaker

By Ward Sinclair
Washington Post Staff Writer

Rep. Dan Glickman (D-Kan.) says he doesn't know who wielded the mystery pencil that changed what he intended, but he'll be in the unusual position today of proposing an amendment to his own pesticide patent protection bill.

Glickman's legislation, the Agricultural Patent Reform Act, is expected to be approved by the House Judiciary Committee and then be rushed to the floor for final action before Congress adjourns in 2½ weeks.

The language that Glickman intends to change apparently would overturn a Supreme Court decision last month that upheld the government's right to disclose health and safety data on pesticides. The case involved the Monsanto Co., which sought to stop the Environmental Protection Agency from making the data available.

The mystery, however, was how the new language got into Glickman's bill. The most likely candidate, the National Agricultural Chemicals Association (NACA), denied that it had any role in the rhetoric ruckus and claimed to be as surprised as Glickman.

"If I knew who did it, I would tell you," said Dr. Jack Early, president of the industry trade group. "I have no idea how that language got in there. It never should have been in there . . . . We have worked with Dan on his bill and somehow there is a misconception of what NACA is doing."

The change in language occurred between last Thursday, when a Judiciary subcommittee chaired by Rep. Robert W. Kastenmeier (D-Wis.) approved the bill, and Monday, when a "clean" version of the bill was made public. The Thursday version had only limited protections of product confidentiality.

"I don't know where that language came from," Glickman said yesterday, "and I'm not sure that NACA had an influence . . . . I'm not sure there's anything so nefarious in this thing and I'm positive that the chairman operated in good faith and wanted to reach an accommodation."

Glickman said he was unaware that his bill contained a secrecy provision until it was pointed out to him and questioned by an environmental lobbyist. The language would permit the manufacturer—not the government—to decide what information could be withheld as a "trade secret or confidential commercial or financial information. Any data so designated may not be disclosed."

Also caught by surprise were EPA officials, who expressed some reservations about the Thursday language because of new hearing procedures it would require the budget-crimped agency to undertake. The new language drew a stronger protest from EPA.

Glickman said that although he was uncertain of the source of the new language, he quickly notified NACA officials "that I did not support that language and they indicated to me that it was not their intention to go around the Supreme Court decision in the Monsanto case. I said that I wanted it changed."

The Glickman bill, moving through Congress at an unprecedentedly quick pace, is controversial for other reasons. It would extend by up to five years the patent protections that pesticide makers now enjoy if their patent term is interrupted by federal premarket safety review requirements.

Glickman, also a member of the House Agriculture Committee, contends the extra time is vital to industry and to agriculture, which urgently needs new pesticides to combat crop damage by insects.

The National Audubon Society and the Environmental Policy Institute, strong critics of the legislation, argue that the bill has been rushed to judgment without adequate hearings and that, contrary to the NACA's arguments, industry profits are not deterred by federal product reviews.

Congressional Quarterly
Aug. 11, 1984--Page 1999

Critics Score Agricultural Drug Bill

Environmental groups are objecting strongly to a bill that would give makers of pesticides and other agricultural chemicals a longer period of patent protection, up to 25 years, for products that must undergo federal approval before they can be sold.

The measure (HR 6034), approved Aug. 8 by a 20-6 vote of the House Judiciary Committee, is meant to encourage companies to invest in the research and development of new, improved products.

But a handful of environmental and consumer groups say that the bill ignores serious health problems associated with the products while giving an unwarranted financial windfall to a highly profitable industry. Jack Doyle of the Environmental Policy Center, in a letter to committee members, said that industry data showed that the costs of research and development for pesticides are recouped within the first year or two of sales, and that pesticide makers are currently reporting record-high earnings.

Maureen Hinkle of the National Audubon Society said she dislikes the bill but hopes to trade support for it to gain enactment of stricter federal controls over pesticide residues in food. Rep. Henry A. Waxman, D-Calif., has introduced pesticide residue legislation (HR 5495) that Hinkle wants to be linked with HR 6034.

Dan Glickman, D-Kan., sponsor of the patent bill, said, "I don't object to linkage, but I make no promises as to whether that linkage will occur. I have not read the Waxman bill. We'll look at it."

The committee accepted an amendment by Glickman to eliminate language that unintentionally overrode an important Supreme Court decision on pesticides. *(Weekly Report p. 1937)*

Senator **Mathias**. Mr. Haddad.

STATEMENT OF WILLIAM F. HADDAD

Mr. **Haddad**. Before I begin my testimony, I suddenly realized this morning why Democrats elect you in Maryland. The analogy to me is how you must feel this morning with President Reagan. I hear patent term restoration praised, but then I hear the substances, no substance, it is like President Reagan announcing that he is for sanctions in South Africa and not following what the Senate recommended. I have that same feeling here, because this is not patent term restoration despite what the Patent Office says. I do not believe the administration supports this bill, not that I have heard. The Patent Office did not support this bill last time; they were the last ones in the hallway here after everybody agreed to a compromise, and it was Commerce and the Patent Office that tried to kill the bill. So I think we have got to clean up the record, to take their statement in the context of experience. I will try to do some of that this morning. With all due respect, Senator, I appreciated your support on the other bill, but I think you will see some of the analogies here, and that might help explain some of the discomfort I feel.

My name is William Haddad. I am vice chairman and chief executive officer of Danbury Pharmacal, a manufacturer of generic drugs. But I am here this morning as chairman of the Generic Pharmaceutical Industry Association which represents the manufacturers of low-cost generic drugs. Our members would like to manufacture, distribute, and sell lower priced generic drugs to vets who service farmers and animal owners, but at the moment, under existing conditions, we cannot. Veterinary patent holders already have what amounts to a de facto monopoly which prevents competition. With all due respect, what you should be considering today in terms of veterinary products is not how to sanction and perpetuate this monopoly, but how to increase competition, as you did last year under the Drug Price Competition Act.

In a phrase, this legislation, I believe, is a disservice to the American consumer and the American farmer who pays the bills. It is a restriction of competition. It is an attempt to achieve in the Halls of Congress what the major pharmaceutical companies, including Eli Lilly, have failed to achieve by research in their laboratory, a practice which I thought we effectively ended last year with the drug price competition legislation which every Member of both Houses, with the exception of Senator Metzenbaum, supported. Although I honestly believed last year that we of the generic industry gave up what was our right, the right to compete when a patent legally expired, for something the brand name companies did not deserve, patent extension, on the argument that the Kefauver-Harris amendments of 1962 had cut patent life in half, I nevertheless enthusiastically supported the compromise which has already, as you know, led to dramatic decreases in pharmaceutical prices.

In 1981, this committee had the delicate facade of an academic study to back up the contentions of the PMA that patent life had, indeed, been cut in half by bureaucratic regulation. I testified then that the study had been covertly financed by the PMA companies and the results structured and twisted to fit a predetermined conclusion. Your committee promised to investigate my charges, but events moved so rapidly that it was not until the legislation had been stalled in the House and a compromise was being formulated that the truth emerged. Patent life had not been cut in half. Yet in the interim, 90 Senators and almost two-thirds of the House of Representatives had been convinced of the study's objectivity. I wonder, Senator, if we are not being treated to the same structured facts today? Certainly there is nothing in the record to justify this legislation in terms of veterinary products.

Let's look at the hard record. I am now a generic manufacturer. A patent on a veterinary product has expired. As a businessman, I want to compete. I cannot. There is no procedure for competition, under law, at the FDA. No procedure under law. I know this sounds familiar to you; that was the situation on post-1962 human drugs. But then we had a facade of a procedure; the paper NDA. No facade of a procedure exists in the veterinary field. Bottom line: I cannot compete. The so-called pioneer company has a perpetual exclusive market. How? Why?

Let us go deeper. A veterinary drug is approved after extensive studies. The FDA approval is followed by 17 or more years of exclusive market life. The patent expires. We are told we cannot compete unless we redo all the original experiments, which is the bureaucratic way of making it impossible. You, personally, with your vote soundly rejected those arguments last year in human drugs. How can we advocate turning back the clock now?

Let us go one step further. On human drugs the PMA companies argued, as they argue today, about research. I will let the record speak on that. But there is virtually no competition in the veterinary field. One in ten drugs has competition. Let me show you what happens with competition. I will submit for the record a longer list.

Metronidazole/flagyl in humans, the price in 1983 was $67 for 100 tablets; the generic price, because that is one where we could compete, was $18. That is what would happen in this industry

What is the push behind this legislation? Senator, I hate to do it, but once again, let me be blunt and to the point. Last year, Senator Hatch and Congressman Waxman promised an effort to extend competition to the veterinary field. Can it be that faced with the inevitability of legislatively mandated competition, some companies concocted a case to extend patent life on drugs which are already part of an ongoing, exclusive monopoly? Certainly no objective facts justify this legislation with regard to animal drugs. Is this a case of protectionism for the big company against the competition?

This is not, to use a congressional phrase, not revenue neutral. Who is hurt? The hard-put farmers of this country. Senator, I was raised with dirt farmers. I campaigned in every State with dirt farmers and, God willing, when I retire, I will be a dirt farmer. I have never met a dirt farmer who would pull on his suspenders and say, "Senator, I will spend $6,000 for something that I can get for $2,000." With all due respect to the distinguished secretary of agriculture from the State of Maryland, I never met a dirt farmer that, given the facts, would act that way.

And who benefits? Who else hurts? You know about the cat and dog owners, they're hurt. And those who raise from animals, they're hurt. And who benefits? A handful of small pharmaceutical companies.

May I make a suggestion? It is the same suggestion you accepted in 1982. Send the bill to objective economists and statisticians. See if it stands the test of truth. Last time, events captured time. When you were away, they passed the bill and the study was not done. We need to find out if the facts presented to you are true. They were not true in the human drug field, and I have a sense they are not true in this field as well.

Finally, competition stirs the juices of the major companies, not only in innovation but in old-fashioned competition. Two major drugs went off patents since you passed this bill: Propranol, which is Inderal, a drug for the elderly. Joe Williams, who is the PMA chairman and CEO of American Cyanamide, benefited when Parke-Davis got a generic approval. And they're now competing at generic prices. The same thing happened on Valium when Lederle got a generic approval and is now tracking generic prices. Competition is healthy for the economy.

As you recall from testimony before you, you have brand generics which sell at a multiple of the generic price. What has happened in this brandnew marketplace is that the major companies are not only tracking us in generics but meeting us in price. This is what we want to happen in the veterinary marketplace. What this legislation proposes is to stall that event. It makes legal what has been de facto.

I urge that Judiciary and Labor solve their turf problems to the advantage of the consumer.

Thank you once again for listening to my diatribe. I feel very strongly about this one, Senator, again because the facts being presented to you, from what I know, are not accurate.

[Prepared statement of Mr. Haddad follows:]

PREPARED STATEMENT OF WILLIAM F. HADDAD

My name is William F. Haddad. I am Vice Chairman and Chief Executive Officer of Danbury Pharmacal, a manufacturer of generic drugs. But I am here this morning as chairman of the Generic Pharmaceutical Industry Association which represents the manufacturers of lower priced generic drugs. Our members would like to manufacture, distribute and sell lower priced generic drugs to vets who service farmers and animal owners, but, at the moment, under existing conditions, we cannot. Veterinary patent holders already have what amounts to a de facto monopoly which prevents competition. With all due respect, what you should be considering today is not how to sanction and perpetuate monopoly, but how to increase competition.

In a phrase, this legislation is a disservice to the American consumer who pays the bills. Further, it is a restriction of competition. It is an attempt to achieve in the halls of Congress what the major pharmaceutical companies, including Eli Lilly, have failed to achieve by research in the laboratories ... a practice which I thought we ended last year with the Drug Price Competition and Patent Restoration Act which every member of both houses, with the sole exception of Senator Metzenbaum, supported. Although I honestly believed last year that we of the generic industry gave up what was our right -- the right to compete when a patent expired -- for something the brand name companies did not deserve ... patent extension based on the premise that the Kefauver-Harris amendments of 1962 cut patent life in half, I nevertheless enthusiastically supported the compromise which has already led to dramatic decreases in pharmaceutical prices.

In 1981, this committee had the facade of an academic study to back up the contentions of the Pharmaceutical Manufacturers Association that patent life had been cut in half by bureaucratic regulation. I testified then that the study had been covertly financed by PMA companies and the results structured and twisted to fit a predetermined conclusion. Your committee promised to investigate my charges, but events moved so rapidly that it was not until the legislation had been stalled in the House and a compromise was being formulated, that the truth emerged. Patent life had not been cut in half. In fact, the average patent life was over 15 years. Yet, in the interim, 90 Senators and almost two-thirds of the House had been convinced of the study's objectivity. I wonder if you are being treated to the same structured facts today? Certainly there is nothing in the history or the record to justify this legislation.

Let's look at the hard record.

I am a generic manufacturer. A patent on a veterinary product has expired. I want to compete. I can't. There is no procedure for competition, under law, at the FDA. No procedure under law. I know this sounds familiar to you, that was the situation on post-1962 human drugs. But then we had a facade of a procedure: The paper NDA. No facade of a procedure exists in the verterinary field. Bottom line: I cannot compete. The so-called pioneer company has a perpetual exclusive market. Why? How?

Let's go deeper. A veterinary drug is approved after extensive studies. The FDA approval is followed by 17 or more years of exclusive market life. The patent expires. We are told we cannot compete unless we redo the tests, go the whole yard, which is a bureaucratic way of making it impossible to compete because of the unnecessary costs involved. You soundly rejected those arguments last year in human drugs when the Price Competition Act was approved. How can you advocate turning back the clock now?

Let's go one step further. On human drugs the PMA companies argued they were spending their profits on research. Congress had already awarded a twenty-five percent tax credit for new basic research. And, as we all know, pharmaceutical companies routinely expense out R & D -- they do not capitalize it as other industries do -- and as a net result, the government ends up paying up to half their research costs. Further, when we gave the PMA companies patent extension, it was to compensate for those research expenditures.

There is virtually no competition in the veterinary field. Only one in ten animal drugs have competition, and even those approvals are riddled with favoritism.

What's behind the push on this one? Once again, let me be blunt and to the point. Last year Senator Hatch and Congressman Waxman promised an effort to extend competition to the veterinary field. The Animal Drug Institute and the FDA have informally commented on this direction. Even the brand name companies and the GPIA seemed to be in agreement either out of belief or necessity.

Can it be that faced with the inevitability of legislatively mandated competition, some companies concocted a case to extend patent life on drugs which are already part of an ongoing monopoly? Certainly no objective facts justify this legislation with regard to animal drugs. Is this a case of protectionism for the Big Company against the competition?

This is not -- to use a Congressional phrase in another context -- this is not legislation that is revenue neutral. Who is hurt and who is helped? The hard-put farmers of this country are big losers. They are paying double and triple for their veterinary products, money that could be used for mortgage, loans or seed. The dog and cat owners of America are also losers. They are paying double or triple for their drugs. Horse breeders, too, pet lovers of all sorts. We're talking about a hidden billion dollar market.

And who benefits? A handful of pharmaceutical companies who won't let go of a good thing. Who won't bend or alter to competition. No one else. I wonder how Congress can defend a different patent bill for every segment of an integrated industry.

May I make a suggestion? It is the same suggestion which Senator Mathias accepted from GPIA in 1982. Send the bill to objective economists and statisticians. See if it stands the light of day. Last time, events captured time. When Senator Mathias was away, the human drug patent extension bill slipped through this committee and after a lot of pain and political aggravation, it was brought back to the Senate where a final compromise was fashioned, a compromise that is working for the consumer and, frankly, for the generic industry. All to the credit of the Congress. Competition has also stirred the juices of the brand name companies and on the two major products which are subject to competition, Propranolol -- Inderal -- and Diazepam -- Valium -- the brand name companies are tracking generic prices, becoming competitive with us. No one would have predicted that Joe Williams' company -- the same Joe Williams who is Chairman of PMA -- that his company, Warner Lambert would become a generic competitor at generic prices. And Lederlie, part of American Cyanamide, is a generic competitor at generic prices, on Propranolol. I stress at generic prices, because the largest drug manufacturers of human generics are brand name companies: Lilly, Pfizer, Parke-Davis, SKF and Lederlie, but until you passed the Drug Price Competition Act, their generic prices were a multiple of our generic prices.

That is what we want to happen in the veterinary marketplace. What this legislation proposes is to stall that event. It makes legal what has been de facto. I urge that Judiciary and Labor solve their turf problems to the advantage of the consumer.

Thank you.

Senator **Mathias**. Well, let me start out by saying that I do not know whether to thank you for your opening remarks concerning some similarities between my approach to the problem and that of President Reagan. But I will take it as a compliment.

Mr. **Haddad**. It was a compliment, Senator. I was trying to identify my feeling with your feeling as I watched you on TV this morning.

Senator **Mathias**. I think that Mr. Doyle has posed a very interesting and a very intelligent series of questions to the committee, and I am glad that the advocates of the legislation, the industry representatives are here still in the room.

And as you heard at the outset, I am keeping the record open for 30 days, and I will hope that we may get some assistance in coping with those questions from the industry witnesses who have appeared. It would be very helpful to the committee to have that assistance. So we will attempt to look at those questions independently, but I think it would be good to have the advocates of the bill also look at those questions and give us the benefit of their views, looking at Dr. Early, among others, in that connection.

Now, since this is not the first time we have talked on these subjects, Mr. Haddad, I can understand the concern that you expressed with such vigor, that the patent restoration for animal drugs should be coupled with an expedited procedure for approving generic animal drugs. And I got the sense of urgency in your voice, the frustration that you did not see any present procedures that answered that purpose.

I have no problem with considering these issues; I think each one of them deserves to be looked at very carefully on its own merit. I do not know that they necessarily have to be tied up in a single bill. The only virtue to that is that you resolve them both at one stroke, if there is certainty that both will be dealt with. They do not have to be in the same bill.

I can understand why there is a desire for a two-tier bill analogous to the 1984 pharmaceutical bill, but we do, of course, then run into a jurisdictional question. And I would like to have your thoughts on that.

If a two-tier bill were introduced, where would it be referred? Perhaps jointly or perhaps sequentially to the Labor and Human Resources Committee and to the Judiciary. What would you think?

Mr. **Haddad**. Last year we did it in the hallway.

Senator **Mathias**. Well, where do you start? You have to start somewhere.

Mr. **Haddad**. Well, last year we started at the back door. We came in through the House. You know, if you want a candid answer. I know the problem, but first of all, I am not convinced—I do not know the chemical side, but listening to the arguments, I am not convinced by them. But assuming that there are compromises as to what was equitable, I think that it could be worked out. I am not sure where the administration is on this bill. I am not sure where FDA is. I know where FDA was last year when Hatch and Waxman talked about it; we left it out of the bill because somebody made a political blunder on behalf of the chemical companies and it did not get included. They took track A when track B won. But I think it can be worked out.

First of all, I am not convinced that they deserve it, but in the sense of compromise, I cannot see how the human drug bill could go ahead and not apply to animal drugs. This bill is worse than what we faced in human drugs, I mean, literally, Senator. One witness told you about a drug that had 21 years of exclusive market life and he bragged about it just a few minutes ago. This is a big market, it's an important market. And we cannot compete. There is no procedure. They tell me at FDA the procedure is tied up by law and we got to untangle that. And then if they want some patent extension, let us do like we did last year; we put in a lot of safeguards, not enough for Senator Metzenbaum, but we put in enough safeguards to make it palatable to Joe Williams of the PMA and also the so-called dissident companies.

Senator **MATHIAS**. Of course, the problem with trying to recreate the situation of last year is that we had a very special situation. We had dual jurisdiction between Human Resources and Judiciary. In order to expedite the agreement that had been reached by the parties most interested, the Judiciary waived its jurisdiction. And whether that is an attainable situation again is, of course, in the moving of time. But obviously we need the help of all the people who are interested in participating. We do not want anybody frozen out of this ball game. Everybody should play a role and see if we can work out something which would be satisfactory and which will move along rapidly, because we are dealing with an evolving economy. We are dealing with farm economy which is in a desperate situation, and we want to make sure that we do not do anything which will be detrimental to a farm economy that is already in very serious trouble. We want to do what we can to give a lift to the farm economy.

So we need everyone's help and everyone's best thoughts on it, good will and a commitment to try and resolve the problem which is perceived by at least some segments of the industry.

Mr. **HADDAD**. Can we hold until we put that together? Last year you were very anxious to make sure that the facts were in before you personally voted on the legislation, but when you were away, Senator Thurmond took the bill and ran with it, and we were left out in the cold and we had to catch it in the House. What assurances this year—if we begin to try to do what we can to find what is an equitable compromise and bring the various parties together—that you may not get called out of town and someone take it and run with it again. That is what our history is, Senator.

Senator **MATHIAS**. Well, I have indicated earlier today that the subcommittee would take no action while we work our way through some of the delicate negotiations that are obviously involved here.

Now, of course, what the chairman of the full committee may do is another matter. As you well know, the Lord giveth, the Lord taketh away.

Mr. **HADDAD**. Well, we would like very much to cooperate with you, Senator. You have always been accessible to us even when you did not agree with us. We have a great deal of confidence in your integrity and ability, and I hope we can find a way through this one, too.

Senator **Mathias**. Thank you very much, gentlemen. We will follow up—yes, Mr. Doyle?

Mr. **Doyle**. If I could say one more thing. I think that something that has not been talked much about here today is that this legislation deals with products made by way of biotechnology. I think that there really is a revolution going on in agricultural research with biotechnology, and you cannot just look at agricultural research budgets now. I think you have to look at life sciences research in several areas and across several fields in these companies. And if you look at R&D investments in that light, there are substantial increases since the early eighties. I might say that I have a book entitled "Altered Harvest" that I have been working on for the last 2 years dealing with agricultural biotechnology that will be published this fall, two chapters of which go into some detail on the patent question. But we feel that if the subcommittee takes a considered look at some of the questions we have raised here—and we welcome the views of industry on these questions—we think some unbiased analysis is needed. And weaving-in the changes coming with biotechnology is very important, especially since biotechnology is mentioned in the legislation. We may be presiding over an era where we are seeing an end to certain pesticide and veterinary type products in the traditional role——

Senator **Mathias**. Well, I think that is a serious——

Mr. **Doyle** [continuing]. To newer kinds of products, and I think we need to pause and really look hard at the patent-life and patent-term now. For if we are at that historic divide, what role will patents, and patents on older products play in stimulating or stymieing innovation.

Senator **Mathias** [continuing]. I think that is a serious area of inquiry. The committee has available to it expert, independent sources of information on the biotechnological field, and we will pursue that.

Mr. **Doyle**. Thank you.

Senator **Mathias**. Thank you very much, gentlemen, for being with us.

The committee will stand in recess, subject to the call of the Chair.

[Whereupon, at 11:44 a.m., the subcommittee was adjourned, subject to the call of the Chair.]

APPENDIX

ADDITIONAL STATEMENTS

STATEMENT OF THE
ANIMAL HEALTH INSTITUTE
TO THE
SENATE JUDICIARY COMMITTEE
SUBCOMMITTEE ON
PATENTS, COPYRIGHTS AND TRADEMARKS

Concerning S. 1093
The Agricultural Patent Reform Act of 1985
September 10, 1985

The Animal Health Institute (AHI) is the national trade association representing the principal U.S. manufacturers of animal health products, including pharmaceuticals, feed additives, and biologics, used in livestock and poultry production and those used to treat household pets, horses, and other species. AHI has fifty-four member companies. AHI's criteria for membership require that each member firm be engaged in ongoing, innovative research.

AHI urges passage of legislation to restore patent life lost during regulatory review of new animal drugs, biologics, and other chemicals. Enactment will restore important incentives for research into animal drugs to maintain the vitality of animal agriculture and an abundant supply of animal-derived foodstuffs.

The 17-year span of patent protection was established by Congress in 1861, and that same patent duration remains in place today. Manufacturers of animal health and nutrition products have found, however, that in reality, usable patent protection exists for much less than 17 years. A substantial amount of this patent protection loss is due to the exceedingly complex systems U.S. regulatory agencies have evolved for pre-market approval of animal health products. New animal drugs cannot be marketed without the prior approval of the Food and Drug Administration; animal biologics must be licensed by the U.S. Department of Agriculture's Animal and Plant Health Inspection Service before they can be marketed in interstate commerce; and pesticides for use on animals must have the approval of the Environmental Protection Agency before they can be marketed. These systems of pre-market approval have provided our nation with a wide array of animal health products with high standards of safety and effectiveness. But the systems are necessarily, and at times overly, time consuming. Over the years, as our knowledge has grown in the biological sciences, statutory and regulatory requirements have expanded.

The Effective Patent Life Is Decreasing

Effective patent-life loss has come about with the expansion of drug approval requirements, starting with the 1962 Kefauver-Harris Amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act). These amendments spawned massive requirements for efficacy data for both human and animal drugs. Patent term losses have become even more extensive over the past decade. In 1973, FDA proposed new scientific standards for the review of potentially carcinogenic new animal drugs, implementing the 1958 Delaney Clause and the 1962 DES Exception, both of which were codified in the 1968 Animal Drug Amendments. This proposal, commonly called the "sensitivity of method" standard (SOM), has been formally revised twice, and has yet, a dozen years later, to be finalized. Nonetheless, it was employed as the scientific standard of review when proposed and has been used ever since. The effect has been dramatically increased review times for new animal drug applications (NADAs) for food-producing animals. (For a decade, the SOM requirements were so stringent that no, or only 1 or 2, NADAs for food-producing animals were approved annually.)

Numerous other causes have been identified by our industry as contributing to the length of the approval process and thus to the diminution of effective patent life. The excessively long periods during which products languish in the regulatory process, especially compared to approval times in nations with comparable regulatory systems, has become known as the U.S. animal drug lag. Since 1980, FDA has taken several steps to reduce the animal drug review time, but substantial reductions simply are not possible under the current system.

Based upon data supplied by 11 AHI member companies in the summer of 1985, recently approved products (i.e., those for which investigational applications were filed after 1973) for use in food-producing animals have lost an average of five years and eleven months of patent life where the patents claim a compound or composition, and three years and eight months of the lives of patents claiming a use. These "recently approved" products are small in number, however — only twenty patents are involved for all 11 companies. More significant are the figures relating to patent life erosion for products that are still awaiting FDA approval. These same 11 firms reported they had NADAs pending for 21 products in June, 1985, with an average compound or composition patent loss already of seven years and seven months. An additional ten products then pending approval, all covered by use patents, had an average patent loss to date of six years and five months. Several of these, of course, were recent filings and had lost less than two years of patent term; however, 17 of the total of 31 covered by product or use patents had lost more than seven years of patent life as of June, 1985.

Here are some specific examples provided by AHI member companies:

For one company, a composition patent on a product was granted in November, 1975, three months after the initial investigational new animal drug (INAD) filing. Approval of this product was granted in September, 1983. Nearly eight years of the product's patent life had already expired. This same product received marketing approval in the United Kingdom in September, 1979. Ironically, this product was granted "fast track" status in July, 1980, by FDA. "Fast track" (formally known as "expedited review") is a system for the priority review of new animal drug applications for innovative, therapeutically-important drugs which are new chemical entities. Approval still took over three years after this drug received fast-track status, despite diligent attempts by its manufacturer to expedite approval. The first European approval of this product was granted in Ireland in January, 1978.

Another company lost nine years of patent life on a product approved in 1982. Patent protection for this product was received in 1972, a year before the company filed its INAD with FDA. The product was approved in the United Kingdom in 1978.

In December, 1970, Pfizer, Inc., received patent protection for Morantel, a wormer for beef and dairy cattle. The INAD on Morantel was filed in July, 1970, and more than 11 years later, in October, 1981, FDA approved the NADA on this product. Close to 11 years of patent protection were lost. This same product received regulatory approval in the U.K. in 1970.

One final example. In 1972, the Upjohn Company filed an INAD on Dinoprost Lutalyse, an agent for regulating reproductive processes. The company received patent protection in the same year. This product was finally approved seven years later, with an equivalent loss of patent protection. This same product was approved in the U.K. in 1975, following a 10-month review period.

These examples clearly and dramatically underscore the lack of adequate patent protection for animal pharmaceuticals. In addition to FDA regulation of AHI member companies' drug products, animal biologics producers are subject to the regulations of the U.S. Department of Agriculture under the Virus-Serum-Toxin Act, and makers of animal pesticides must adhere to the rules of the Environmental Protection Agency under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Toxic Substances Control Act (TSCA) to manufacture and market their products. As it should be, partial patent term restoration in all these areas is covered by the proposed legislation.

In 1981, the Senate passed legislation (S. 255, 97th Congress) originating in the Subcommittee on Patents, Copyrights and Trademarks, which would have provided up to seven years of patent term restoration for the products covered by S. 1093, as well as some other products. In 1982, that legislation was also approved by a majority of the House of Representatives, but the bill (H.R. 6444, 97th Congress) was considered under suspension of the rules, and the vote was five votes short of the two-thirds majority required for passage under that procedure.

The inequity of the situation is starker today than in 1981. Today, for some categories of products subject to FDA pre-market approval patent term restoration is a reality. Congress has recognized the basic unfairness of the present system to researchers and innovators who face a pre-market approval system. Now that the principle has been recognized, it should be applied fairly to all categories of products that are similarly situated.

Societal Benefits of this Legislation

In addition of the equitable aspects of the legislation, the long term benefits to society should not be overlooked. Animal health products fall into four major categories: biologics which provide immunity to disease; dosage-form pharmaceuticals which are used to treat, prevent, or control disease; animal feed additives which are used to curb disease and to improve feed efficiency by reducing the time and amount of feed needed to bring farm animals to top market weight; and animal pesticides, which rid animals of parasites.

Animal vaccines and other biologics and dosage-form pharmaceuticals help livestock and poultry producers minimize disease losses. Animal scientists estimate that the livestock industry suffers a 20% loss annually from diseases; obviously, more research needs to be done, but great strides have been made, as evidenced by losses of more than 50% per year in some less-developed countries.

Animal feed additives are of great economic importance to livestock producers. These products give producers the capability to obtain maximum efficiency from the resources available. Thus, they are a major factor in making abundant supplies of meat and poultry products available to consumers at reasonable prices.

The public health aspects of animal disease prevention cannot be ignored, either. There are over 150 zoonotic diseases, i.e., ones that are common to man and other animals. Some, such as rabies, can be controlled by animal vaccination; others, such as brucellosis, still evade eradication.

These are serious animal disease problems which threaten the economic lives of livestock producers and pose risks to human health. Much more needs to be done to develop treatments for viral diseases and the difficult-to-treat bacterial diseases, such as brucellosis. The animal health industry is poised to attack now-incurable diseases and to find preventions or cures that are safer and more effective than the products now available.

The animal health products industry is heavily committed to working toward these goals. Based on a survey of 1984 sales, the Animal Health Institute estimates that domestic net sales of animal health products totalled just over $2 billion. The survey also provides the estimate that U.S. companies (AHI member and non-member firms) spent over $251 million on research and development of animal health products in 1984. Thus, R&D investment totalled over 12.5 percent of sales. AHI estimates that about 84 percent of the R&D is "innovative" research aimed at development of new products, with the remainder being "defensive" to demonstrate the continued safety and effectiveness of already-approved products.

Despite the drastic losses of effective patent life, animal health product manufacturers have continued to invest heavily in new products. However, innovation has clearly suffered. As a practical matter, the drug developer must assume that a newly-discovered product will have only 10 years of patent-derived marketing protection. R&D can be devoted only to a product with a potential market sufficiently large to recoup the investment in 10 years, instead of the 17 years that innovators in other fields enjoy. Current estimates from another AHI study indicate that the R&D costs for a new drug for a food-producing animal are in the range of $14 to 16 million. The market must be large to recover such an investment (and the investment in chemicals tested that do not lead to marketable products) and yield a profit in a short time. Another four or five years of patent protection would allow the recovery of the investment with a product of significantly lesser volume. If the current situation is unchanged, R&D aimed at products for less common diseases or diseases in the less common species will continue to diminish.

The animal health products industry will not go bankrupt or fail to develop any new products if the status quo is maintained. Rather, the effect will be a very limited rate of innovation, with efforts focused on the segments of the market which have the potential for high returns and high-volume sales.

Specific Comments on S. 1093

AHI supports the approach to patent term restoration taken by S. 1093, but we note that the legislation would provide only partial restoration of time potentially lost due to federal pre-market review of the products involved. There is a "cap" in S. 1093 which would limit the amount of restoration to a maximum of five years, even if the regulatory review period runs a great deal longer. As described below, AHI believes the other "caps" in the legislation are redundant and unnecessary.

Regulatory Review More Than Ten Years After Patent Applied For. Subsection 156 (a)(3)(A) of the bill would permit patent term restoration for only one half of the regulatory review time occuring more than ten years after the patent application is filed, and there would be no restoration for regulatory review occuring beyond twenty years from the filing of the patent application. AHI recommends that these limitations be deleted. The cost of lost patent protection is the same regardless of when the regulatory review period occurs. Any concerns about an patent holder's failure to actively pursue clearance of the product by FDA, EPA, or USDA are addressed by the "due diligence" provisions in subsection (b)(2) and the cap on maximum restoration.

Twenty-Five Year "Cap". Subsection (a)(3)(B)(iii) provides that the term of a patent would expire not later than 25 years from the date of the filing of the first U.S. patent application, including any extension. This provision would work to the disadvantage of patent applications that require a long review period before being granted, and product applications that require a long regulatory review period would be disadvantaged. We fail to see the equity of this additional "cap" and recommend that it be deleted from the legislation.

Active Ingredient in a Product. The present language of Sec. 156(a)(1) of the bill would authorize the extension of a patent claiming a product, method of manufacture of a product, or method of using a product. As defined in subsection (c)(1), it would appear that "product" means the finished form of drug or pesticide. In AHI members' experience, however, the product's developer is often able to patent a new active ingredient but is not able to patent the finisned product. We recommend that the legislation state explicitly that a patent is eligible for extension if it claims an active ingredient in a product, or a method of using an active ingredient in a product, or a method or manufacturing an active ingredient in a product.

Method of Manufacturing Using Recombinant DNA Technology. Subsection (a)(1)(D) contains limitations on the eligibility for extension of patents claiming a method of manufacturing a product, with separate limitations for patents primarily using recombinant DNA technology. Innovative methods of manufacturing products, involving recombinant DNA or not, are extremely important to the efficient production and delivery of animal health products. AHI does not think that the limitations in subsection (a)(1)(D) are warranted and recommends that those provisions be deleted from the bill. This would bring the treatment of patents claiming methods of manufacture into conformity with the provisions of the patent term restoration law for human pharmaceuticals.

Products Under Review At Time of Enactment. Subsection (a)(3)(B)(iii) would provide that, if a product is under review at the time of the enactment of this legislation, the maximum patent term restoration allowed would be three years, and there would be no restoration allowed for regulatory review time occuring prior to the date of enactment. We recommend that the limitation of restoration to post-enactment regulatory review time be deleted. All products that are in the "pipeline" at the time of enactment should be treated the same. An application filed five years prior to enactment but not approved until after enactment should be as eligible for the three-year "pipeline" restoration as application filed two months before enactment.

Major Health Effects Tests. Subsections (c)(5)(B) and (C) define the regulatory review period for pesticides and agricultural and other chemicals to include time prior to filing an application during which the sponsor is undertaking a "major health or environmental effects test," as defined in subsection (c)(2). Quite often, the sponsors of new animal drug products likewise conduct extensive health or environmental testing prior to the product being tested under FDA's investigational rules. Therefore, it is equally appropriate to include the time of major health or environmental effects tests in the regulatory review period for new animal drug products, as defined in subsection (c)(5)(A). Similarly, we recommend that subsection (a)(3)(B)(i) be revised to recognize that the regulatory review period for new animal drugs include the time for major health and environmental effects tests conducted for a new animal drug application that was found to have insufficient data.

Conclusion

Research and development within the agricultural drug and chemical industries have aided significantly in making large-scale production of livestock and poultry possible. However, new and improved drugs and biologics need to be developed to combat now-incurable diseases and to find preventions or cures that are safer and more effective than the products now available. Unfortunately, investment in the research and development of products such as animal drugs and biologics that require lengthy governmental approval is discouraged by shortened patent lives. A decline in the number of new animal drug introductions has paralleled the decline in real patent life and must be reversed. Increasing research incentives will stimulate the development of new and improved dosage-form drugs, feed additives, and biologics for the livestock and poultry industries to use to reduce the billions of dollars they now lose to disease and condemnations. Improved products to enhance the health of companion animals will also result.

As as result of the 17-year patent clock ticking away during the regulatory approval process, a significant portion of the expected patent term that rewards innovation and research is lost for important new animal drugs, pesticides, and biologics. By correcting this inequity in the patent system, the pending patent term restoration legislation will enhance incentives for research into the development of significant new products to benefit the livestock and poultry industries and the owners of pets. These new products, through improvements in animal husbandry, will ultimately benefit the American consumer.

THE TEXAS AGRICULTURAL EXPERIMENT STATION
THE TEXAS A&M UNIVERSITY SYSTEM
College Station, Texas 77843-2147

Office of the Director
(409) 845-8484

May 31, 1985

TO: Neville P. Clarke

FROM: Melvin J. DeGeeter

SUBJECT: S 1093 Agricultural Patent Reform Act
HR 1069

We owe a vote of thanks to Senator Mathias (MD) and the cosponsors Thurmond (SC), Biden (DF), DeConcini (AZ), Heflin (AL), Denton (AL), and Specter (PA).

An overview of S 1093 is:

- Patent restoration would be available for animal drugs, animal biologics, pesticides, and toxic chemicals.

- Up to five years of patent restoration would be available on products that are the subject of applications filed after the effective date of the bill. Products with applications in the "pipeline" at enactment would be eligible for up to three years of patent extension.

- There would be a "cap" on the patent extension, with the maximum period being 25 years from the date the patent application was filed.

- Subject to these limits, the bill would credit the full amount of the "regulatory review period" occurring during the first ten years following the submission of the patent application; one-half the review period occurring during the next ten years would be credited.

- A provision would authorize USDA, FDA, and EPA to charge user fees to recover the costs of (1) calculating the regulatory review period for a product and (2) responding to a petition which challenges the agency's determination of the regulatory review period (including the costs of any hearing or other proceedings). This provision was in the House agricultural PTR bill last year, but there is no comparable provision in the PTR/generic human drug bill enacted in 1984.

- Application for patent extension must be within 60 days after approval, which is limited time to assess actual market potential.

An overview of HR 1069 is:

- Push is on for process patent legislation--companies in a variety of industries have formed a coalition to promote legislation which would expand the protections of the patent law for process patents. One bill on the subject (H.R. 1069) has been introduced so far, sponsored by Rep. Carlos Moorhead (R-Calif.), the senior Republican on the House Judiciary Subcommittee on Courts, Civil Liberties, and the Administration of Justice, which has jurisdiction over patent bills.

- Under current law, if a copy of a patented product is sold or used in the United States without the patent owner's approval, the seller or user can be sued for infringement. That is the case for a patented process only if the process is used within the United States. If a person uses the process to make a product overseas, without the patentholder's consent, that product can be sold or used in the United States without subjecting the seller or user to a patent infringement suit. The only remedy for the holder of a process patent is to ask the U.S. International Trade Commission (ITC) for relief. The remedy available is the exclusion of the product from this country, after a long and expensive proceeding. No monetary award to the injured party is available in an ITC proceeding.

- H.R. 1069 would give the holder of the process patent the right to sue for infringement when a product made overseas by unauthorized use of the patented process is sold or used in the Untied States. There is opposition to the legislation from the generic human pharmaceutical industry, which argues that it would discourage the importation of drugs and raise drug prices. As a result, there is the possibility that pharmaceuticals will be dropped from the bill. More intraindustry disputes are expected to arise, as individual companies examine the effects of specific legislative language on their products.

Texas Agricultural Extension Service

The Texas A&M University System
College Station 77843

Office of the Director

May 31, 1985

MEMORANDUM

TO: Mr. Michael Lytle, Special Assistant to the Chancellor for Federal Relations

SUBJECT: S.1093, AGRICULTURAL PATENT REFORM ACT

Federal testing requirements for pesticides needing approval as a requisite to commercial marketing have been expanded substantially during the past two decades. The testing requirements increasingly address health and environmental concerns reflecting new knowledge obtained through experience and through advances in science and technology.

Similar developments have evidently affected federal testing requirements of veterinary biological products, animal drug products and animal antibiotic products as well. Extending the term of patents for such products to account for time lost on a patent in meeting these testing requirements as proposed in S.1093 appears to represent a needed acknowledgment of changing times.

Both the private and public sector (including universities) stand to benefit should their work result in product, use or process patents on one or more of these chemicals. Providing equity through extending patents covering these chemicals should stimulate greater research and innovation as suggested by Senator Mathias (Congressional Record May 7, 1985, S.5548).

Differences, assumed to reflect the consensus of views explored through the legislative process, in determining the period of extension are evident upon comparison of the legislative history of PL 98-417 with S.1093. One of the features of S.1093 relating to the period of extension appears questionable. S.1093 provides that no term of any extended patent may exceed 25 years, a period in excess of the normal 17-year term of a product, use or process patent. As the maximum extension possible is 5 years, it would appear that the 25-year period stated is in error. Additionally, it seems unlikely that the intent of the bill is to provide an extension beyond the normal 17 years of market exclusivity.

Sincerely,

Z L Carpenter
Zerle L. Carpenter
Director

RECEIVED
JUN 05 1985
CHANCELLOR'S OFFICE

ZLC:ms

CORRESPONDENCE

GENERAL COUNSEL OF THE
UNITED STATES DEPARTMENT OF COMMERCE
Washington, D.C. 20230

6 SEP 1985

Honorable Strom Thurmond
Chairman, Committee on the
  Judiciary
United States Senate
Washington, D.C. 20510

Dear Mr. Chairman:

Thank you for your letter requesting our comments on S. 1093, the "Agricultural Patent Reform Act of 1985," which extends the principles of patent term extension to agricultural and industrial chemicals and to animal drugs. The legislation is patterned on, but is not identical to, the patent term extension provisions applicable to pharmaceuticals under the "Drug Price Competition and Patent Term Restoration Act of 1984" (Public Law 98-417) which the Administration strongly endorsed.

Extending the life of a patent to compensate its owner for patent life lost due to pre-market regulatory procedures preserves the vitality of the patent system as a means of encouraging innovation and scientific advancement in a manner that reflects the obligation of Federal agencies to protect the American people from products that are unsafe or of doubtful efficacy. The concept is not peculiar to pharmaceuticals. There is no reason why it should not be extended to these chemicals and drugs.

Although S. 1093 achieves this purpose, it contains a number of objectionable features which compel the Administration to withhold endorsement. All of these, fortunately, are easily correctible as the enclosure, which has been prepared under the direction of Acting Commissioner of Patents and Trademarks Quigg, indicates.

As the enclosure reveals, our principal concern lies with the bill's potential for deterring persons from undertaking important research and development activities or from disclosing valuable scientific information about innovation. Neither result would be consistent with the principles and purposes of the patent system. The bill is deficient in this respect in that it (a) "rations" patent rights by denying extension to a patent owner based on other patents which that person owns or controls or on the existence of earlier patents on related technologies; (b) discourages patent owners from trying to find new uses for their patented products; and (c) may discourage further research on products using certain active ingredients.

There are also a number of technical drafting problems which the enclosure describes in considerable detail. In brief, the bill (a) uses a very complicated formula for determining the period of patent extension when its purposes can be achieved far more simply by counting the entire regulatory review period and placing a cap thereon; (b) permits patent term extension for chemicals and drugs that receive approval for marketing prior to enactment; (c) may place us in potential violation of the Paris Convention for the Protection of Industrial Property in the way it requires us to treat foreign priority dates; (d) does not provide that the duties of the Commissioner in this area should be purely ministerial; (e) unnecessarily requires the Patent and Trademark Office to adopt different administrative procedures for processing pharmaceutical patent extensions and agricultural chemical patents; and (f) fails to reflect the Administration's commitment to the principle that users of the patent system should pay for its operation.

Each of these is, as noted, easily corrected - in most cases either by incorporating parallel provisions from Public Law 98-417 or by deleting parallel provisions that, in our view, should not have been included in that statute.

The Office of Management and Budget has advised us that there is no objection to submission of this report to the Congress from the standpoint of the Administration's programs and that enactment of this legislation, if suitably amended, would be consistent with its policies

Sincerely,

Douglas A. Riggs
General Counsel

Enclosure

DETAILED COMMENTS ON S. 1093, THE "AGRICULTURAL PATENT REFORM ACT OF 1985."

Section 157(a)(1)(D) of S. 1093 provides a complicated formula for determining a patent's eligibility for extension if it claims a method for manufacturing a product. A distinction is made between patents claiming a conventional process and those which claim the use of recombinant DNA technology. In both instances, the owner of the process patent cannot also own a patent for the product or for a method of using the product. In addition, a conventional process patent is not eligible for extension if the owner was issued an earlier patent claiming another conventional process of manufacturing the product. In the case of a patent claiming the use of recombinant DNA technology, that patent is only eligible for extension if no earlier patent exists, regardless of ownership, claiming the use of recombinant DNA technology in the manufacture of the product.

This approach is unfair. A newly discovered process for making a product may well represent a scientific and commercial breakthrough. The owner of a patent claiming such a process should not be denied extension of a patent on the basis of other patents he owns or controls, nor should the existence of earlier patents to related technologies have any bearing on the merits of extending a particular process patent which was denied a full and effective term due to Federal premarket regulatory review.

This is not the first time that the Senate has considered and rejected this approach. During the 98th Congress, a similar approach was contained in an early version of the "Drug Price Competition and Patent Term Restoration Act of 1984" (S. 2748), but was omitted in the bill as passed by the Senate (S. 1538), and as finally enacted into law (P.L. 98-417). We urge, therefore, that S. 1093 be modified to omit the complicated formula appearing in section 157(a)(1) (D), and that the simpler and fairer approach of 35 U.S.C. 156(a)(5) (B) be adopted. Further, section 157(a)(3)(C) already provides that only one patent may be extended for the same regulatory review period for any product.

Section 157(a)(1)(E) permits, with one exception, extension for patents relating to products or their use only if the regulatory review resulted in the first permitted commercial marketing or use. The exception exempts patents claiming a method of manufacturing products with the use of recombinant DNA technology. We question the wisdom of this policy that would deny extension to later patents which disclose, for example, new and unobvious uses for a previously approved product. Such a policy does not lend encouragement to the owner of a product patent to invest the sums needed for research and development to find new uses for his already patented product. It would seem only fair to allow patent term extension for subsequent patents which disclose new use inventions.

Sections 157(a)(3)(A) and (B)(iii) would establish a formula for the length of time for which a patent term may be extended. For regulatory review during the first ten years from the filing date of the earliest patent application, full credit would be given toward patent term extension. Between ten and twenty years from that filing date, only half the regulatory review period would count toward extension. Finally, no term could exceed 25 years from the earliest filing date of the application. Since S. 1093 already contains a five-year cap of maximum allowable patent term restoration, we would have preferred the simpler approach of counting the full regulatory review period up to a fixed number of years toward obtaining an extension of the patent term. This is especially so, since the formula expressed in section 157(a)(3)(A) --taking into account regulatory review periods for patent term extension before any patent has issued-- is apparently contradicted by the last sentence of section 157(c)(5), which states that no regulatory review period shall be deemed to have commenced until the patent to be extended has been granted.

Further, section 157(a)(3)(A) refers to "the date of filing of the earliest application" which triggers the running of the first ten-year period. This date is defined in section 157(c)(3) as being the one "providing the earliest benefit of a filing date to the patent and includes patent applications under section 120". This definition, however, is not limited to applications under section 120 and, therefore, includes foreign priority filings. Such a requirement may be in conflict with the Paris Convention for the Protection of Industrial Property, which provides that a foreign priority date may not be considered in the allocation of the length of a patent term. Accordingly, we prefer the definition of the earliest application for a patent to be the same as that spelled out in section 157(a)(3)(B)(iii) of the bill, namely, "the earliest United States patent application which provides support under section 120 of this title for any claim of the patent to be extended".

Section 157(a)(3)(B)(iii), however, is unclear in several other aspects. The third sentence telescopes the concepts of patent term extension and regulatory review period into one. To avoid confusion, we would suggest the following wording as a substitute: "If the regulatory review period for a product began before the date of enactment of this section and if on such date the regulatory review period has not ended, it shall be measured from the date of enactment and the period of extension for the patent shall not exceed three years." Further, the legislation should also clarify how patents should be treated for which such review ended before enactment. The present wording of this section would permit the same length of patent term extension for these patents as it would provide for patents for which the regulatory review period began only after the date of enactment. This is not consistent with the bill's less generous treatment of patents for which regulatory review began but did not end before enactment.

Another point concerns the language of section 156(a)(3)(D). This section is unclear as to whether it would provide patent term extension for a product having two or more active ingredients where only one of these ingredients had been claimed in a previously extended patent. We believe it would be unwise to deny patent term extension to compositions with multiple active ingredients solely on the basis that one of those ingredients was protected by a patent which had already been extended. The product covered by the previously extended patent can be used by all upon expiration of the patent. To deny patent extension to another product simply because it includes one ingredient which was claimed in an earlier extended patent would serve as a disincentive to further research on products using that ingredient -- a result contrary to the purposes of the bill.

An important consideration concerns the duties of the Commissioner of Patents and Trademarks under this legislation. For example, section 157(b)(3) requires the Commissioner to specify

in the certificate of extension any claim to which such extension is applicable. Although the product sponsor is required by section 157(b)(1)(E) to identify in the notification the particular claim involved, we would prefer section 157(b)(3) to state that, when issuing a certificate, the Commissioner may rely solely on the information contained in the notification referred to in section 157(b)(1). Such language would clearly reflect that the Commissioner's duties are purely ministerial. This change would considerably reduce the costs to the Office to administer patent term extension applications in the field of agricultural and industrial chemicals. Further, false information furnished by the applicant for extension could be used as a defense to defeat any infringement action by the owner of the extended patent. And lastly, section 156(e) of title 35, United States Code, already addresses these duties of the Commissioner when issuing a certificate of extension for pharmaceutical patents.

It would be in the interest of the public, as well as in the interest of Federal agencies and departments involved in the administration of patent term extension, if procedural aspects of legislation providing for extension of agricultural chemical patents were harmonized to the extent possible with existing law providing for extension of pharmaceutical patents. In some instances, applicants for extension of pharmaceutical patents are the same as those applying for extension of agricultural chemical patents. Procedural uniformity would certainly lessen the burden on applicants and agencies alike.

For example, in detailing the elements which an application for extension of a patent relating to a human drug product shall contain, section 156 (d)(1)(E) of title 35, United States Code, provides for the furnishing of the patent or other information as the Commissioner may require. Further, 35 U.S.C 156 (d)(4) provides that "[a]n application for the extension of the term of a patent is subject to the disclosure requirements prescribed by the Commissioner". It would be useful to add such provisions also to the requirements of what a notification for extension under section 157 (b)(1) should contain, in order to assist the Commissioner in carrying out his duties.

Finally, we note that section 157(b)(2)(G) permits the Secretary and the Administrator to establish fees to cover the costs involved in carrying out their duties under this bill. Although the duties of the Commissioner of Patents and Trademarks may not be as extensive as those of the Secretary and the Administrator, we urge that the Commissioner also be authorized to establish fees covering the costs of processing notifications for patent term extension. Such an authorization is consistent with the policy of charging the users of the patent system with the costs for its administration and, incidentally, is also included in 35 U.S.C. 156(h), in the case of applications for pharmaceutical patent extentions.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 9 1985

OFFICE OF
EXTERNAL AFFAIRS

Honorable Charles Mathias, Jr.
Committee on the Judiciary
United States Senate
Washington, D.C. 20510

Dear Senator Mathias:

Thank you for providing the Environmental Protection Agency (EPA) the opportunity to comment on S.1093, the "Agricultural Patent Reform Act of 1985." This letter is being sent to you in lieu of testimony for your September 10, 1985 hearing on that bill.

S. 1093 would restore the term of the patent grant, in the case of certain products, for the time a regulatory review period prevented the marketing of the product. As it relates to EPA, this bill would provide for extension of certain patents involving pesticides and chemical substances within the jurisdiction of the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). S. 1093 would apply where the effective use of the products subject to the patents has been delayed by regulatory reviews which must occur under these Federal laws before the products in question can be produced or used.

EPA has historically supported the notion of patent term extensions for products regulated under FIFRA and TSCA. It is clear that several years of patent life can be lost while the appropriate reviews are made under FIFRA and to a certain extent under TSCA. Thus EPA generally supports the intentions of the bill. However, because the provisions of S.1093 would impose certain duties on EPA, we are providing the enclosed detailed comments on matters of concern to assist the Committee in its consideration of the bill.

The Office of Management and Budget has advised us that there is no objection to the submission of this report from the standpoint of the President's programs.

Sincerely,

Richard E. Sanderson
Acting Assistant Administrator
for External Affairs

Comments of the Environmental Protection Agency on S. 1093 "Agricultural Patent Reform Act of 1985"

1. Our first comment relates to the title of the bill, "Agricultural Patent Reform Act of 1985." This title is misleading in that the bill potentially affects hundreds of new industrial chemicals regulated under the Toxic Substances Control Act (TSCA) which have nothing to do with agriculture. We suggest the following title: "Agricultural and Industrial Chemicals Patent Reform Act of 1985."

2. In paragraph (a)(1)(B) the words "pursuant to statute" should be deleted. The regulatory review periods that are the subject of the legislation are defined in paragraph (c)(5) of the bill. In the case of TSCA, the regulatory review period is defined as reviews under section 5 of TSCA (paragraph (c)(5)(C) of the bill). Section 5 of TSCA creates two kinds of regulatory reviews. The first is mandatory, by operation of section 5(a)(1)(a) of TSCA, for all new chemical substances. The second, a significant new use rule under section 5(a)(1)(B) and (2) of TSCA, is not imposed automatically by operation of the statute. It results from a rulemaking. The usage of the words "pursuant to statute," in the absence of legislative history to the contrary, could be read as restricting the bill to regulatory reviews required by statute, unnecessarily limiting patent extension for uses of products or manufacturing methods subject to a significant new use rule under TSCA. We believe the purposes of the bill are best served by including regulatory reviews under TSCA section 5(a)(2) significant new use rules within its coverage.

3. We recommend that paragraph (c)(5)(C) of the bill, which defines the regulatory review period for TSCA, be changed as follows. The references in paragraphs (c)(5)(C)(i) and (ii) to section 5(e) and 5(f) of TSCA should read:

> ... or if an order or injunction is issued under section 5(e) or 5(f) of such Act which prohibits the production of the substance or prohibits its specific use, ... [additional language underscored]

Orders and injunctions under section 5(e) and 5(f) of TSCA are regulatory tools which can be used to control activities with a new chemical substance or activities relating to a significant new use when EPA identifies unreasonable risks resulting from those activities. Section 5(e) of TSCA allows EPA to prohibit or limit the manufacture, processing, distribution in commerce, use, or disposal (or any combination of these) of a new chemical substance or such activities relating to a significant new use of a chemical substance when EPA finds the activities may present an unreasonable risk of injury to human health or the environment or when the substance will be produced in substantial quantities with significant or substantial human exposure or substantial environmental release. Most of the orders issued by EPA under section 5(e) do not prohibit outright the manufacture or use of the substances in question. EPA has issued many "consent orders" under section 5(e) (agreed to by the regulated companies) which merely limit manufacturing, processing, distribution in commerce, use, and disposal of the substances by requiring certain controls on human exposure and/or environmental release during manufacture, processing, use, and disposal of the substance. Thus such orders generally do not prevent a patent holder from being able to manufacture and use its product. (Section 5(f) orders, on the other hand, are used solely to prohibit such activities.) The new language recommended above would draw the distinction between orders or injunctions which prohibit activities, and thus leave the patent holder unable to profit from its product, and those which merely impose reasonable controls on such activities. If the language of the bill is not changed as recommended above, a patent holder which is fully able to market its product (albeit with certain controls), and thus able to profit from it, would still be entitled to patent extension. We do not believe this is consistent with the intent of the bill which apparently seeks to compensate the patent holder for the time when its product cannot be produced or used during the regulatory review.

4. The bill may provide broader patent extension than intended. Frequently, developers of chemicals obtain patents which cover a group of related chemical structures, often several hundred, and the claim relates to the use of those substances. Typically the patent holder actually uses only a handful of the structures commercially. Different substances covered by the patent may be marketed separately over time. We forsee a problem with respect to patents covering substances subject to reviews under section 5 of TSCA. Any chemical substance manufactured or processed for commercial purposes, other than research and development, prior to June 1979 was placed on the Inventory of chemical substances maintained under section 8(b) of TSCA. TSCA defines a "new chemical substance" as any chemical substance not on the Inventory. Such substances must be reviewed under section 5 of TSCA before they can be manufactured and used. The problem with the bill arises from the following situation:

> Assume a manufacturer holds a patent which covers the use of a hundred related substances. Prior to 1979 some of those substances were put into commercial production and were placed on the TSCA Inventory. They would not be subject to review under section 5 of TSCA, and the manufacturer would be free to manufacture and use them without restriction. If the manufacturer later decided to manufacture and use another substance subject to the same patent after June 1979, the substance would be a new chemical substance subject to review under section 5 of TSCA. After completion of the review, the manufacturer could apply for an appropriate extension of the patent under the bill.

The terms of the bill are ambiguous at best as to whether the extension would apply to the entire patent, including the substances which had been freely manufactured and used without a regulatory review, or only to that portion of the patent which applies to the substance which was the subject of the regulatory review. We believe either the bill or the legislative history should clarify the situation to provide that the extension would apply only to the claim for the specific substance in the patent which was the subject of the regulatory review.

5. The final problem with the bill relates to the issue of confidentiality of business information. Section 10 of FIFRA and section 14 of TSCA contain detailed provisions concerning confidentiality of information and how EPA may use and disclose such information. Paragraph (b)(4) of the bill attempts to address this issue for the patent extension. However, it raises several problems.

First, by way of background, many new chemical substances submitted for premanufacture review under section 5 of TSCA are claimed as confidential, even when they are the subject of a patent. (This is most likely to occur when the patent is of the type, described in our comment 4 above, covering a class of related substances. EPA has been informed by industry that in this situation, the identity of the specific substance, which is chosen from among all those subject to the patent, to be commercialized is the secret.) Further information about the use of the substances and other information reported to EPA is also often subject to confidentiality claims. Under TSCA, EPA keeps such information confidential and identifies the substances in any publications or public documents by generic chemical names and premanufacture notice numbers, even after manufacture begins. (This is unlike the situation with drugs and pesticides where the identity of the active ingredient is disclosed to the public when it is registered or approved.)

Under the bill, a person seeking patent extension for a new substance subject to section 5 of TSCA or a pesticide under FIFRA would apply to the Patent Office (paragraph (b)(1)). The Patent Office would then ask EPA to determine the applicable regulatory review period. EPA would make the determination and would be required to publish notice of the determination in the Federal Register (paragraph (b)(2)(A)). Under the structure of the bill, this notice would be the first notice to the public that patent extension was even being sought. If EPA received a petition arguing that the product sponsor did not act with due diligence during the review period, EPA would be required to make a determination as to due diligence and publish a notice of that determination (paragraph (b)(2)(B)). Finally, if requested, EPA would be required to hold an informal hearing on the due diligence issue and publish a final Federal Register notice of the final determination (paragraph (b)(2)(C).

These provisions would be undercut by the provisions of paragraph (b)(4) of the bill. That paragraph would limit disclosure in connection with patent extension for pesticides and new substances under TSCA to disclosure which would be allowed under section 10 of FIFRA and section 14 of TSCA. Neither of those provisions was written with a patent extension process in mind.

In addition to the problems above, paragraphs (b)(3) and (b)(4) of the bill may be inconsistant as they apply to TSCA and FIFRA. Paragraph (b)(3) of the bill requires the Commission to identify the product. This may be inconsistent with paragraph (b)(4), because in certain cases TSCA and FIFRA treat the identity of a product as a protected trade secret. We therefor recommend that paragraph (b)(4) be amended to conclude with the proviso "except as provided in (b)(3)."

We have also been informed that, with respect to patent extension applications received for drugs, food additives, and medical devices under the newly enacted 35 U.S.C. 156, the Patent Office places such applications in a public file. The language of paragraph (b)(4) of S. 1093 would appear to prohibit such an action for chemical substances which are claimed confidential under TSCA. (Other information in such an application for either a new chemical substance under TSCA or a pesticide might have also been claimed confidential and kept so by EPA.) If the Patent Office cannot disclose such information publicly, EPA could not in turn disclose it in any of the three Federal Register notices discussed above which would be required by the bill. Further, it would be difficult, if not impossible, to hold a hearing on due diligence if the information about the matter must be kept confidential.

We believe that a different confidentiality provision must be incorporated into the bill. Such a provision should provide that, if a person seeks extension of the term for a patent covering a specific chemical substance, its use, or its method of manufacture, the application and the information contained in it would not be confidential for purposes of the patent extension process. (This is consistent with the thrust of the patent system under which, in exchange for protection of novel inventions, patent holders release information about those inventions.) Further, the provision should provide specific direction as to whether information not included in the application, but which is relevant to determining the regulatory review period and the due diligence of the product sponsor, which may have been claimed confidential, can be revealed in the course of making determinations about the review period and due diligence. In the absence of a provision which allows such disclosure, the Federal Register notices of determinations by EPA could be very uninformative. In addition, it would be difficult for a third party to effectively challenge due diligence and receive a fair hearing before the Agency. Read literally, the provision might even prevent EPA from communicating effectively with the Patent Office on these matters.

If the Committee believes that the due diligence provision is necessary, the confidentiality rules must be adapted to it.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 13 1985

OFFICE OF
EXTERNAL AFFAIRS

Honorable Charles Mathias, Jr.
Committee on the Judiciary
United States Senate
Washington, D.C. 20510

Dear Senator Mathias:

This letter is in response to your letter of November 5, 1985 which raised questions regarding the impact of S.1093, the proposed patent term extension legislation on EPA's regulatory activities. The responses to these questions are enclosed.

Thank you for providing the Environmental Protection Agency the opportunity to provide comments on S.1093, the "Agricultural Patent Reform Act of 1985."

The Office of Management and Budget has advised us that there is no objection to the submission of the enclosed responses from the standpoint of the President's programs.

Sincerely,

Joy Manson

Jennifer Joy Manson
Assistant Administrator
for External Affairs

Enclosure

Question 1

To what extent do patents generally, and patent term extension in particular, contribute to the product lifetime and economic entrenchment of products that may be dangerous to the public health and safety and protection of the environment? Once patented, is it more difficult to effectively regulate and, if necessary, recall dangerous products from the marketplace?

Answer

We do not believe that patents or patent term extension have or will have any impact on the product lifetime and economic entrenchment of products that may be hazardous to the public health and safety and protection of the environment. Virtually all pesticides are patented but such patents do not affect EPA's regulatory activities or prevent EPA from acting promptly to deal with any problems that may arise.

Question 2

What effect will enactment of this patent term extension bill have on the pesticide regulatory process? Will it expedite that process or make it slower?

Answer

We do not believe that the enactment of the patent term extension bill in its current form will have any effect on the pesticide regulatory process per se, neither expediting nor slowing it. However EPA may have to perform certain functions relative to patent term extension, such as determining the regulatory review period and making findings concerning the patent holder's "due diligence" during the regulatory review time period. We are unable to predict the resource requirements which these functions may impose.

Question 3

If this legislation (S. 1093) is adopted, what will be the combined effect of these patent term extension provisions with certain patent-like and exclusive use provisions now found in the pesticide laws?

Answer

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) provides a registrant a period of exclusive use of certain data submitted to support a registration and a period during which the registrant must be compensated if its data are used to support another person's application for registration. We believe that the time period of such exclusive use and compensation requirements will, in most cases, coincide with the period during which a patent is in effect for such pesticide.

National Corn Growers Association
WASHINGTON OFFICE
Suite 201
1015 - 15th Street, N.W.
Washington, D.C. 20005
202/371-1450

1985 SEP 25 PM 2:35

The Honorable Charles McC. Mathias, Jr.
Senate Judiciary Subcommittee on Patents,
Copyrights, and Trademarks
Room 198 RSOB
Washington, D.C. 20510

September 23, 1985

Dear Mr. Chairman:

The National Corn Growers Association would like to express its support for S.1093, the Agricultural Patent Reform Act, which provides equitable patent rights for agricultural chemicals.

Under current statute, new agricultural chemicals undergo rigorous and extensive scientific review and testing prior to EPA approval, substantially reducing the 17-year patent term available to other products which are not required to meet federal testing standards prior to commercial use. Clearly, such requirements are extremely important to ensure safe and effective use.

At issue, therefore, is the serious disincentive a shortened patent term may have on a company which must risk a significant amount of research and development capital in the discovery, approval and marketing of new and more effective agricultural chemicals. As a result of these staggering investment costs, patent protection becomes an important consideration for any company deciding whether to take the risk of developing an agri-chemical product from which they may not recover these significant outlays before other manufacturers can begin to market the same or similar products.

American agriculture is dependent on competitively priced and readily available chemical products. The NCGA is hopeful that by providing patent term restoration, agri-chemical manufacturers will continue to aggressively pursue and develop new chemical products that apply to changes in productive technology while reducing costs to farmers over the full life of the patent.

Thank you for your leadership on this important issue. We look forward to working with you on this important legislation.

Sincerely,

Varel Bailey

Varel Bailey
President

VB:mj
cc: Subcommittee Members

IPO INTELLECTUAL PROPERTY OWNERS, INC.

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Melvin P. Williams
United Technologies Corp
Hartford, CT

EXECUTIVE DIRECTOR

Herbert C. Wamsley
Washington, DC

October 10, 1985

The Honorable Charles McC. Mathias, Jr.
Chairman, Judiciary Subcommittee on Patents,
Copyrights and Trademarks
United States Senate
Washington, DC 20510

Dear Senator Mathias:

I am writing on behalf of Intellectual Property Owners, Inc. (IPO) to urge passage of S. 1093, the "Agricultural Patent Reform Act".

IPO is a nonprofit association whose members own patents, copyrights and trademarks. Our members include large corporations, small businesses, universities and individuals. Our members include companies from most of the major fields of American industry.

IPO believes the incentives provided by the U.S. patent system are responsible for much of the research and development conducted in this country. A major factor affecting the strength of patent incentives is the length of the patent term.

Testimony has been presented to your subcommittee showing that the effective length of the patent term for agricultural chemical inventions is many years shorter than the 17 year patent term enjoyed by other inventions. The effect of Federal regulatory review on patent life for agricultural chemical inventions was never foreseen or intended by the Congress.

IPO believes the benefits of patent protection should be available to the same extent for innovators in all fields of technology. Any other policy not only is unfair but deprives the American public of the benefits of new technology in the fields adversely affected.

S. 1093 also would strengthen competition in the agricultural chemical industry. The stronger incentives provided by restored patent terms would make available in the marketplace a greater variety of new and improved products, and these products in many cases would compete with products already on the market. In the long run this would mean lower prices for consumers and a stronger national economy.

The reasons why the legislation is needed apply with equal force in the case of animal drugs, which are also covered by S. 1093.

We hope your Subcommittee will approve S. 1093 at an early date.

Sincerely,

Donald W. Banner

Donald W. Banner
President

Grain
The voice of
Maryland's grain industry

Maryland Grain Producers Association, Inc.
c/o Willard Chemical Company
P.O. Box 180, Frederick, Md. 21701

Senator Charles McC. Mathias Jr.
387 A Russell SOB
Washington, DC 20510

Dear Sir,

I am writing concerning the Agricultural Patent Reform Act Senate Bill 1093. I am Allen Davis, a farmer from Kent County, Maryland. and President of the Maryland Grain Producers Association.

I,m writing on behalf of the Maryland Grain Producers. I will state that we are strongly in favor of the Agricultural Patent Reform Act Senate Bill 1093.

As a farmer, I have appreciated the research and develppement that the Agri-Chemical Companios have conducted toward creating pesticides that have helped the American Farmer to reach the production goals he has today. However, their future involvement in the production of Agri-chemicals can only be considered temporary unless this bill is passed. Their financial risk is simply not a feasible one unless the patent term is restored.

Farmers are now realizing a stranger dependence on newer and safer chemicals for the future, much more than in the past. We have environmental groups looking for fewer chemicals to be applied, while soil conservationists are encouraging no-till farming which depends heavily on chemicals to kill the pests that tillage has controlled in the past. These are challenges that demand a cooperative effort between the farmer and the Agri-Chemical Producer, and as a result I feel that we will all benefit.

Thankyou for considering our position and it is our hope that you will pledge your support for this bill..

Sincerely yours,

R. Allen Davis

R. Allen Davis
Pres. Maryland Grain Producers Asso.

CAST®

COUNCIL FOR AGRICULTURAL SCIENCE AND TECHNOLOGY

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November 13, 1985

American Academy of Veterinary and Comparative Toxicology
American Dairy Science Association
American Forage and Grassland Council
American Meat Science Association
American Meteorological Society
American Phytopathological Society
American Society for Horticultural Science
American Society of Agricultural Engineers
American Society of Agronomy
American Society of Animal Science
Aquatic Plant Management Society
Association of Official Seed Analysts
Council on Soil Testing and Plant Analysis
Crop Science Society of America
Institute of Food Technologists
North Central Weed Control Conference
Northeastern Weed Science Society
Plant Growth Regulator Society of America
Poultry Science Association
Rural Sociological Society
Society of Nematologists
Soil Science Society of America
Southern Weed Science Society
Weed Science Society of America
Western Society of Weed Science

The Honorable Charles McC. Mathias, Jr.
387 Russell Senate Office Building
Washington, D.C. 20510

Dear Senator Mathias:

Thank you for your letter of October 31 regarding S. 1093, the "Agricultural Patent Reform Act of 1984," which proposes to extend the period of patent coverage for certain agricultural products. I claim no personal expertise in your subject, but I shall do the best I can to respond to your questions.

Since publication of Reports 85 and 87, which you say you have, CAST has published no further work on the impact of government regulations on the development of agricultural chemicals. The chairman of the task force that produced these two reports is Dr. Vernon W. Ruttan, Department of Agricultural and Applied Economics, University of Minnesota, St. Paul, Minnesota 55108. His telephone number was 612-376-3560 the last time I called him. He is far more knowledgeable than I, and you may wish to contact him directly.

Now being printed, however, is a report entitled "Plant Germplasm Preservation and Utilization in U.S. Agriculture" that deals in part with the United States Plant Variety Protection Act, which was passed in 1970 by the U.S. Congress. The purpose of this Act was "To encourage the development of novel varieties of sexually reproduced plants and to make them available to the public, providing protection available to those who breed, develop, or discover them, and thereby promoting progress in agriculture in the public interest." We shall send you a copy of this report as soon as it is available, because although it does not deal with agricultural chemicals, it reviews the results of studies that have been made to investigate the impacts of the Plant Variety Protection Act.

The CAST report on plant germplasm is relevant to S. 1093 in another way in that your bill includes provisions on recombinant DNA technology. The use of recombinant DNA technology is something we can look forward to in the future in plant variety development. As far as I know, however, no varieties yet on the market have been developed with use of recombinant DNA technology.

I know of two scientists who have made analyses of the impacts of the Plant Variety Protection Act. One is Dr. L. J. Butler, Department of Agricultural Economics, University of Wisconsin, Madison, Wisconsin 53706. He was a member of the task force that produced the CAST report on plant germplasm now in press. His telephone is 608-263-3212. The other is Dr. Richard K. Perrin, Department of Economics and Business, North Carolina State University, Raleigh, North Carolina 27695. His telephone is 919-737-2608. For information direct from the experts, you should contact these men.

Now, to comment on the questions raised by Mr. Doyle to which you directed my attention, I respond first to question 1. Mr. Doyle asks if there are unbiased economic data showing that product innovation in pesticides and animal drugs has declined recently. CAST Reports 85 and 87 are the only sources of economic data I know about that relate to product innovation in pesticide and animal health products other than the reference Mr. Doyle made to a report in "Chemical Week." I do not attempt to follow this area, and I have not read the "Chemical Week" article to which Mr. Doyle refers, but I would say that Mr. Doyle's statement is consistent with the fact that herbicides are now the biggest market in pesticides. Consequently, it is to be expected that manufacturers would be placing emphasis on herbicide development. As to the lack of economic bias in the data in CAST Reports 85 and 87, I would say that there is bound to be some bias because the returns are not complete. There may be other biases also. But one must stop where the data stop. The reports used the available data.

Mr. Doyle's question 2 asks, in effect, how long does it take manufacturers to recoup their research costs for pesticides and animal drugs, and how do manufacturers make their calculations to answer this question. I suspect this question is unanswerable. The length of time obviously would be variable. Manufacturers are characteristically close-mouthed about such matters, the reason being that the products are proprietary, and they don't want to give their competitors too much information. Statistical data are hard to come by in pesticides and animal health products.

Mr. Doyle's question 3 asks about the profitability of the pesticide and animal drug industries. It is my understanding that there is no place where this information has been collected, but that if such information were sufficiently important, a well qualified person could obtain a pretty good estimate of the profitability by sifting through scattered information in places such as the annual reports companies put out.

Mr. Doyle's fourth question has to do with the product areas in which manufacturers specialize. I think such information could be developed with sufficient effort because the products companies produce are not corporate secrets. As a nonspecialist in the subject on which you are working, however, I do not perceive the relevance of the information in question to S. 1093.

Mr. Doyle's fifth question has to do with the rate of innovation and new product introduction in highly concentrated submarkets. The rate of new product introduction in the total markets has been so low (see CAST Reports 85 and 87) that it must be essentially zero in highly concentrated submarkets.

Mr. Doyle's seventh question is on the potential of patents for stifling research on biological alternatives. Our Report No. 106 on plant germplasm says that the intent of the Plant Variety Protection Act was to stimulate plant breeding research and development. Such an expectation would be reasonable because the patent-like protection would provide the developers an expectation of financial returns over a period of 18 years. On general principles, it would seem that S. 1093 also should provide some impetus to development of competing products.

Mr Doyle uses the term "biological alternatives," however, which I understand to mean nonpesticidal means of pest control and nondrug means of animal health maintenance and enhancement. The connection between S. 1093 and such research seems to me to be rather tenuous, an important reason being that development of pesticides and drugs is essentially the province of the private sector, and development of biological alternatives is essentially the province of the public sector. It is my impression that the support of such work in the public sector is largely a consequence of pressure from the environmental lobby and would have little or nothing to do with length of the patent period for pesticides or animal drugs.

Mr. Doyle's eighth question has to do with foreign and domestic pricing policy on pesticides and animal drugs. The purpose of the companies that make these products is to turn a profit, and for this reason it would be reasonable to infer that the companies would attempt to price their products so as to make the maximum profit in all the markets they enter. This could well involve price differentials in different markets. Information of this sort should be available because companies cannot hide their prices, but I doubt that it has been collected, and I do not perceive its special relevance to S. 1093.

In his introductory statement in paragraph 1 on page 2, Mr. Doyle expresses concern for the economic burden S. 1093 could impose on farmers and ranchers. As I understand it, one of the impacts of S. 1093 would be to increase the costs of pesticides and animal drugs to farmers and ranchers. But according to the CAST task force that produced the report on plant germplasm now in the press, this probably is not the issue. As noted by the task force in connection with plant variety protection:

> An increase in seed prices should not necessarily be regarded as an unexpected or undesirable result of the PVPA [Plant Variety Protection Act]. Indeed, one of the purposes of the PVPA is to permit seed companies to recoup fair returns on their investments in research and development of new plant varieties. It may also be presumed, since the intent of the PVPA is to encourage new and novel varieties of better quality, that farmers would be willing to pay more for 'better' varieties. The issue, then, is not merely a change in prices, but whether or not plant variety protection has triggered structural changes that create or are likely to create sustained unjustifiably high prices.

In its final paragraph on the impact of plant variety protection on seed prices, the task force wrote as follows. I quote this paragraph in full because it seems to me that the content has some relevance to S. 1093:

> It is difficult to evaluate precisely the influence of the PVPA on the seed trade and society in general because so many other factors are involved. It can be safely concluded that the PVPA has had a positive impact on private plant breeding efforts in several crops, but that it has not triggered massive investments in private plant breeding. There is little evidence that substantial public costs have resulted from the PVPA. The influence of the PVPA on increases in seed prices, market concentration and advertising, declines in information exchange and public plant breeding, genetic vulnerability, and loss of plant germplasm resources has been either nil or modest. Thus it appears that the PVPA has resulted in modest private and public benefits at modest public and private costs. If a reasonable balance is maintained between the public and private sectors in the breeding of most crops, the present balance of benefits and costs should continue.

I appreciate your writing and hope you will contact us again if you think we may be of assistance. As you may have judged from CAST Reports 85 and 87, CAST is an educational organization, not a lobbying group. Whereas all the persons whose testimony you sent with your letter took definite stands and tailored their remarks to fit their stands, the CAST Board of Directors does not adopt a position on any of the topics it authorizes for task force effort, and task forces also avoid expressions of support or opposition.

Sincerely,

Charles A. Black

Charles A. Black
Executive Chairman of the Board

c: Mr. Borden

IMPACT OF GOVERNMENT REGULATIONS ON DEVELOPMENT OF CHEMICALS USED IN ANIMAL PRODUCTION

Council for
Agricultural Science and Technology
Report No. 85
October 1980

TASK FORCE MEMBERS

Vernon W. Ruttan (Chairman of the task force), Department of Agricultural and Applied Economics, University of Minnesota

Samuel R. Aldrich, Agricultural Experiment Station, University of Illinois

Thomas Allen, Texas A&M University Agricultural Research and Extension Center at Vernon

Arnold P. Appleby, Department of Crop Science, Oregon State University

Gerald A. Carlson, Department of Economics and Business, North Carolina State University

Don A. Dillman, Department of Rural Sociology, Washington State University

David Graham, Forest Insect and Disease Management Unit, U.S. Forest Service, Washington, D.C.

Ronald J. Kuhr, Agricultural Experiment Station, Cornell University

Charles A. Lassiter, Department of Animal Science, North Carolina State University

Edward C. Naber, Department of Poultry Science, Ohio State University

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John D. Radewald, Department of Nematology, University of California at Riverside

Duane E. Ullrey, Department of Animal Science, Michigan State University

Robert J. Weir, Litton-Bionetics, Kensington, Maryland

Eldon I. Zehr, Department of Plant Pathology and Physiology, Clemson University

FOREWORD

As the Nation enters a period of increasing financial stress, due in part to government actions, including those taken by regulatory agencies, members of the public are becoming increasingly aware that the cost-benefit concept has application to government regulations. Regulations have benefits, but they also have costs. Through education regarding such matters, society will hopefully be enabled to adopt a position in which the benefits are well in excess of the costs.

Because of a desire to increase the general level of understanding regarding the impacts of government regulations on the development of agricultural chemicals, the executive committee of the Council for Agricultural Science and Technology (CAST) authorized the distribution of a mail ballot to members of the board of directors in November 1978 to determine whether a task force should be established to prepare a report dealing with the impacts. The board approved, and the task force was promptly established. The task force included expertise in agricultural economics, agronomy, animal science, dairy science, entomology, meat science, nematology, plant pathology, poultry science, range management, sociology, soil science, toxicology, and weed science.

This report, the first of two prepared by the task force, deals primarily with regulation of animal drugs and nutritional supplements and to a minor extent with pesticides used in animal production. The second report will address the regulation of chemical pesticides used in agriculture and forestry.

The first draft of this report was reviewed by a subcommittee of the task force at a special meeting, and a revised version was sent to the headquarters office for editing. Editing was done by Dr. T. C. Byerly with assistance from the headquarters office, and the edited version was returned to the task force and the CAST executive committee for review and comment. A revised version was then returned to the same groups for further comments before the final version was reproduced for publication.

On behalf of CAST, I thank members of the task force and all the others who gave of their time and talents to prepare this report as a contribution of the scientific community to public understanding. Thanks are due also to the employers of task force members who made the time of their employees available at no cost to CAST. And finally, thanks are due to members of CAST. The unrestricted contributions they have made in support of the work of CAST have financed the report.

This report is being distributed to the Agriculture Committees of Congress, the U.S. Department of Agriculture, the Food and Drug Administration, the media, and institutional members of CAST. Individual members may receive a copy on request.

The report may be republished or reproduced in its entirety without permission. If republished, credit to the authors and CAST would be appreciated.

Charles A. Black
Executive Vice President
Council for Agricultural
Science and Technology

PREFACE

This is a report of the Council for Agricultural Science and Technology (CAST) task force on the Impact of Government Regulation on the Development of Agricultural Chemicals. The task force has organized and focused its efforts in two areas: (a) the effects of regulation on innovation in chemicals for use in animal production and (b) the effects of regulation on innovation in development of plant protection chemicals. The task force decided fairly early in its deliberations not to include a consideration of regulation and innovation in fertilizers.

This report has been prepared by the task force subcommittee on Animal Production Chemicals. It has been read and approved by the entire membership of the task force.

The task force held meetings on January 29 and 30, 1979, in Washington, D.C., and in Atlanta on April 17 and 18, 1979. The two subcommittees each held additional meetings to discuss and revise their findings. The task force held discussions with staff members of the Food and Drug Administration (Bureau of Foods and Bureau of Veterinary Medicine), the Environmental Protection Agency, the USDA Food Safety and Quality Service, the National Agricultural Chemicals Association, the American Feed Manufacturers Association, the Animal Health Institute, the Fertilizer Institute, and the Environmental Defense Fund. Consultations were held with individual government, industry, and university scientists by individual task force members. The task force has appreciated the interest and cooperation of the representatives of government, industry, public interest groups, and individual scientists who have made the report possible. Any errors or misinterpretations of the information incorporated in this report are, however, the task force's own responsibility.

The Subcommittee on Chemicals Used in Animal Production included Charles A. Lassiter (Chairman), Gerald A. Carlson, Edward C. Naber, Albert M. Pearson, Duane E. Ullrey, and Robert J. Weir. The Subcommittee on Chemical Pesticides for Crop and Forest Uses included Eldon I. Zehr (Chairman), Samuel R. Aldrich, Thomas Allen, Arnold P. Appleby, Gerald A. Carlson, Don A. Dillman, David Graham, Ronald J. Kuhr, John D. Radewald, and Robert J. Weir.

Vernon W. Ruttan
Task Force Chairman

SUMMARY

Extensive progress has been made over the last several decades to satisfy the national concern for the health and safety of consumers of animal products. This progress, however, has not been made without costs in terms of reduced productivity of scientific and technical effort devoted to research on, and development of, chemicals for animal production. The decline in research and development productivity has certain unfavorable implications for the future in terms of animal production and cost of animal products to consumers. The principal concerns discussed in this report regarding the system of regulation, the direction in which it is moving, and its consequences may be summarized in the following four points. Some of these concerns are shared also by certain members of the Food and Drug Administration.

- The share of sales devoted to research and development in the animal drug industry appears to have declined since the mid-1970s. The percentage of research and development expenditures devoted to innovation has declined. The costs of developing and testing new animal drugs have risen sharply. The productivity of research and development effort in the animal drug industry has declined. If taken individually, these trends might not appear to be a source of undue concern. Taken together, they imply a less healthy environment for technical advance in the animal drug industry currently than in the past.

- The data requirements for clearing new chemicals are now extensive and are expensive to fulfill, and the process of obtaining clearance is at times unduly prolonged. A clear implication of two case studies presented in this report is that only a part of the delay in obtaining clearance is due to scientific or technical considerations. Major causes of delay include the failure of the Food and Drug Administration to publish the procedures required for clearing new drugs; complex, imprecise protocols for new animal drug applications; step-by-step consideration of the information submitted; and requests for supplemental information.

- The Food and Drug Administration's proposed "sensitivity of method" document does not adequately discriminate between compounds that merit extensive testing and those that do not. The result may be misallocated scientific resources and deterred development of useful chemicals of limited market potential. The document also proposes the use of models which would confound the interpretation of research findings and in some instances would lead to incorrect conclusions.

- The regulatory procedures employed by the Food and Drug Administration discourage the development of both major drugs for minor species and minor drugs for major species of animals. The logical consequence is a direction of research and development in animal health, nutrition, and production toward the major species, and possibly also the concentration of effort on a limited range of products. The ultimate effect could be a failure to utilize effectively the available chemical and genetic potential that will be needed as new sources of productivity in the future.

OVERVIEW

Chemicals are important factors in the production of meat, milk, and eggs. Their use assures more abundant supplies at lower prices to consumers. Food products of animal origin provide about 65 percent of the protein we consume, in forms we prefer.

Through regulatory action, the Food and Drug Administration (FDA) and other federal, state, and local agencies assure the safety and wholesomeness of these foods. Chemicals must be approved for use, and food products from livestock and poultry are monitored for residues of drugs and pesticides as a safety precaution. Residues hazardous to human health are found only infrequently. Regulatory actions are taken to eliminate violative products and their causes. Such actions include the withdrawal of approved drugs found unsafe under conditions of use.

Safe and effective new chemicals are needed to increase animal productivity. New products result from innovative research and development (R&D) carried on in the laboratories of industry sponsors, and in those of public and private research agencies. Publicly supported R&D in agriculture is estimated to yield an annual return to the public of more than 35%. The return to industry and, hence, the stimulus to develop new products, is determined by market returns and costs of product development and marketing. The animal drug industry spent funds equal to 10 to 13.6 percent of annual sales for R&D during the 1965-1978 period.

The number of new animal drugs approved from 1965 through 1967 was 10; only 5 were approved from 1975 through 1977. The cost per new drug, in deflated dollars, increased from $13.8 million in 1965-1967 to $36.4 million in 1975-1977.

Uses of new animal drugs (NADs) and other feed additives for the production of animals and animal food products that move in interstate commerce are subject to approval by FDA under the provisions of the Federal Food, Drug, and Cosmetics Act (FFDCA). States and local agencies may regulate uses for animals and animal products within their respective jurisdictions.

Requirements for approving new drugs and other feed additives are complex and imprecise. In some instances, several years elapse between the time of application and FDA action approving the proposed use. The process of approving new animal drugs could be accelerated and made more efficient if the information to be required were clearly specified in writing at the beginning of the process and if some allowance were made for the changes in requirements that are introduced after the manufacturer has committed resources to obtaining the information specified initially. Changes in requirements may result, not only from new developments in regulations, but also from differences in interpretations and personal views as new FDA personnel become involved in the approval process. Other factors contributing to delay and increasing costs include requirements for establishing safety and efficacy, and for developing and validating methods for quantitative assay of residues and metabolites.

FDA receives New Animal Drug Applications (NADAs), petitions for affirmation of GRAS (generally regarded as safe) status of substances which will become food components, and feed additive petitions. All require information as to the chemical nature of the substance; the safety of the intended use for the health of humans and other animals; the efficacy of the substance for the intended use; and the availability of sensitive, quantitative methods for determining residues in food. NADAs and food additive petitions require environmental impact analyses under the National Environmental Policy Act, administered by the Environmental Protection Agency.

FDA regulations provide that if the FDA Commissioner finds no grounds for denying approval within 180 days after a NADA has been filed, or 90 days after an application has been made for approval of feed containing new animal drugs, the applicant shall be notified that the application is approvable. Ninety days after filing, food additive petitions must be approved, denied, or extended for not more than 180 days.

Despite these provisions, approval has sometimes required much longer. In one instance described in detail, more than 28 months elapsed between application and approval of NADAs for the feed use of one antibiotic drug. A supplemental NADA providing for extended use of the antibiotic to market weight of the recipient animal required 38 months for approval.

Costs associated with approval for use of the nutrient selenium as a feed additive have exceeded 1 million dollars. A case study of the selenium issue shows that requests to FDA for GRAS status for this nutrient, essential for all animals, was requested in 1970; the first feed additive regulation became effective in 1974. Selenium addition to cattle and sheep feeds was not approved until 1979. Losses due to selenium deficiency in cattle and sheep were estimated to exceed $500 million in 1975. There is still no approval for use of selenium in diets of hens producing eggs for human consumption.

The potential market for minor drugs for major species and of all drugs for minor species is currently insufficient to justify the cost of obtaining information required for their approval. Nonproprietary chemicals similarly have too limited a profit potential to justify the costs of obtaining approval for their use.

FDA is cognizant of, and responsive to, needs and opportunities for reduction in cost of approval which do not reduce assurance of safety to human health. Changes in regulations by FDA to make application protocols more concise and exact might reduce the time and cost imposed on applicants without diminishing assurance to consumers of the safety of animal food products.

Publicly funded R&D might provide the data necessary for NADAs for minor drugs, drugs for minor species, and nonproprietary chemicals. In terms of increased supply and variety of foods of animal origin at less cost, the return to the public would likely be high.

A BVM "Medicated Feed Task Force" has recommended that animal drug regulation concentrate on preventing introduction into the human food supply of drug residues harmful to human health. The task force recommended that drugs be classified into risk categories. Drugs posing very small risk might require no regulation. Drugs posing potential residue risk to human health (e.g., carcinogens) would require regulation. Adoption by FDA of the Medicated Feed Task Force proposals could reduce costs associated with NADAs.

Also under consideration by FDA is a "Sensitivity of Method" document. The proposals in this document do not adequately discriminate between compounds that merit extensive testing and those that do not. The result may be misallocated scientific resources and deterred development of useful chemicals of limited market potential. The document also proposes the use of models which would confound the interpretation of research findings and in some instances would lead to incorrect conclusions.

INTRODUCTION

Prior to the mid-1920s, technical progress in American agriculture was directed primarily to the achievement of increases in output per worker through advances in mechanical technology. During the last half century, advances in mechanical technology have been complemented by new biological and chemical technologies directed to increasing output per unit of land, water, and animal resources. Agricultural research and development associated with the technologies has a very high annual return in relation to its cost (Evenson et al., 1979).

Use of chemicals in animal production plays an important role in a livestock industry that provides eggs, milk, and meat to the human diet. Food products of animal origin provide about 65 percent of the protein we consume, in forms we prefer. Drugs are utilized by the producer of animal products to prevent and control various diseases of livestock and poultry, thus enhancing the general well-being of the animal and improving the efficiency of feed conversion. Pesticides are used to control external parasites. The native supplies of essential nutrients in the plant products used for animal feed are supplemented by additional sources used as feed additives to provide adequate nutrition. As a result of the beneficial effects of these chemicals, the animal producer is able to reduce significantly the cost of production, thus contributing to the economic welfare of the producer and providing the consumer with lower cost animal products.

Since the early 1960s, the implications of the new biological and chemical technologies for the health and safety of agricultural producers and consumers and for the quality of the environment have been of heightened concern. The result has been the emergence of new laws and regulations to achieve more effective social control over the development and use of biological and chemical technologies. Regulations to assure the safety of animal products have evolved piecemeal and involve effort by several governmental agencies.

Both the drive for *technical innovation* leading to improvement in the productive capacity of plants and animals and the drive for *institutional innovation* resulting in constraints on the development and use of the new technologies have been generated by powerful economic and social forces. Increasing scarcity of land and water resources, reflected in rising agricultural land values and rising costs of land improvement, is continuing to create a strong need for yield-increasing technologies in agriculture--for higher output per acre. The rising value that society is placing on health and the rising demand for environmental quality have led to a demand for effective social controls over the development and use of new technology.

This report attempts to assess the impact of the new regulatory regimes that have emerged in recent years on innovation in chemical technologies useful in animal production. This is only a small part of the broader issues referred to in the preceding paragraph. The report is dedicated, however, to the proposition that it is in the interest of society to develop a set of institutions to manage the new scientific and technical potential opened up by advances in the application of biological and chemical technology on agricultural production in a manner that permits us to satisfy both the need for advances in agricultural productivity and our concerns for the health and safety of agricultural producers and consumers. It is in the further interest of society that both of these objectives be accomplished in a manner consistent with a good quality environment.

UNIQUENESS OF ANIMALS IN SAFETY OF FOOD SUPPLY

It is a common misconception that all drugs and environmental contaminants fed to food animals are passed *in toto* to humans. The fact is that animals generally pass on only a part, and in some instances almost none, of these substances in the food products that they generate; this provides a unique protective mechanism, a matter that has received little recognition. The problems from contamination have usually been recognized in animals before they became apparent in the human population and have provided a safeguard that is not available in plant products that are consumed directly by humans. An example of this was seen in the recent accidental mixing of polybrominated biphenyls (PBBs) into the rations of farm animals in Michigan, where the problem first became apparent in the animal population (Selikoff et al., 1978). Although deaths were reported in dairy cattle, there was no clear evidence of health problems in the human population (Selikoff et al., 1978). PBB studies by Fries et al. (1978), Durst et al. (1978), and Willett and Durst (1978) have indicated the effectiveness of cattle in filtering PBBs out of the food supply, whether it be milk or meat.

Similarly, aflatoxins were first observed in poultry being fed naturally contaminated feeds (Sargent et al., 1961; Delongh et al., 1962), and later in other species (Allcroft and Roberts, 1968; Keyl and Booth, 1971; Armbrecht et al., 1971). Polan et al. (1971) have shown that only 0.17 to 0.30 percent of the aflatoxin intake could be recovered from the milk of dairy cows. Furtado (1979) has recently demonstrated that retention of aflatoxins in the tissues of the pig amounted to only 0.015 and 0.005 percent of the ingested amounts of aflatoxins B_1 and B_2, respectively. Thus, animals provide a unique and effective filter, as well as a warning of contamination, that has helped humans by either filtering out part of the contaminants or by causing signs of toxicity in the exposed animal population that have aided in recognition of the problem. This protective mechanism was not present in an incident in India in which 106 humans died from eating corn containing aflatoxin that had been produced by the mold, *Aspergillus flavus* (Krishnamachari et al., 1975). The Food and Drug Administration has established "action levels" for aflatoxins and PBBs in feed and food to assure safety (Food and Drug Administration, 1978).[1]

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[1] Action levels represent the limit at or above which FDA will take legal action against a product to remove it from the market.

COMPLEXITY OF THE REGULATORY SYSTEM

The evolution of feed safety requirements through a series of Congressional legislative actions has resulted in involvement of several independent government agencies and the development of several independent sets of regulations governing different aspects of approval for the use of chemical technologies and enforcement of safety requirements for animal products. Consequently, the process of gaining approval for new chemical technologies is often confusing.

Animal products are supervised by four different federal agencies, namely, the Food Safety and Quality Service (FSQS) of the U.S. Department of Agriculture, the Bureau of Foods (BF) in the Food and Drug Administration (FDA), the Bureau of Veterinary Medicine (BVM) also in FDA, and the Environmental Protection Agency (EPA) as well as state agencies (under the Public Health Services Act). Feeds entering interstate commerce are regulated by FDA. States also regulate feeds under state laws. The primary responsibility of FSQS is surveillance and enforcement of regulations to assure that the meat and poultry inspection programs meet standards for food safety and quality. Although FSQS has little input into developing standards for safety, it has primary responsibility for enforcing standards for residues, once they have been adopted. BVM has administrative responsibility for approving new drugs and other feed additives, with regard to both efficacy and animal safety. BF is charged with scientific review of the data on human food safety and, thus, has responsibility for approving drugs and other feed additives leaving residues that enter the human food supply. EPA has the responsibility for approving pesticides utilized primarily for controlling external parasites that could result in residues in animal products. Separate approvals for a new chemical technology thus may be required from more than one agency, and regulations related to animal products must ultimately be enforced by still another agency, FSQS.

The agencies themselves have recognized that the separation of responsibilities has resulted in problems of approving new products for use with food-producing animals. Thus, the Interagency Liaison Group, which is composed of the directors of the several agencies, has been formed to coordinate and clarify the roles of the respective agencies in order to eliminate unnecessary duplication in requirements and functions.

PRODUCTIVITY OF ANIMAL DRUG INNOVATION

The regulatory system has been amazingly effective in assuring a safe and nutritious supply of animal products for human diets. Nonetheless, the cumbersome nature of the system has certain unfavorable impacts on development of new chemical technologies, the consequence of which is not immediately apparent to members of the public.

Research and Development (R&D) expenditures by the animal drug industry expanded in real terms until 1974. This long-term expansion resulted in approval of many valuable compounds. However, the numbers of new compounds approved have declined in recent years. This section examines research productivity of the animal drug industry for the past 15 years and discusses alternative explanations for the recent decrease in animal drug innovation.

Since 1965 the Animal Health Institute (AHI) has compiled information from member companies on their sales, research and development expenditures, and number of new compounds approved. This information is shown in Table 1 for the period 1965 to 1978. An accounting firm is utilized to maintain the confidentiality of the information.

The sales figures for the AHI members are shown in Column 1. There appears to be a steady increase in undeflated industry sales. The annual growth rate has been about 9.4 percent (Column 2) including price increases. Only in recent years has AHI compiled unit prices for representative animal health products. Figures for 1975 and 1976 (not shown) indicate stable prices relative to consumer prices and other agricultural production costs (Animal Health Institute, 1978, p. 22).

Research and development expenditures in nominal and deflated terms are shown in Columns 3 and 4, respectively. Though undeflated R&D expenditures have risen for the industry, the deflated figures in Column 4 show no increases in these investments after 1974. There appears to have been a period of R&D expansion until 1971 and then a relatively constant investment level thereafter. The ratio of R&D expenditures to sales (Column 5) appears to have risen, peaked in 1971, and declined slightly in recent years.

Companies were asked to give the proportion of their R&D expenditures devoted to innovative activities. Though this information is sketchy, it does show a decline in the early 1970s and stability in recent years (Column 6).

The last two columns give a measure of the output of the research and development efforts. Column 7 is the number of new drug entities approved for use in each year, and Column 8 is the total number of animal species for which the new compounds were registered. Although there is considerable year-to-year variability in new compounds registered, moving averages show a reduction in new compounds registered in recent years. Selecting beginning, mid, and ending three-year periods, for example, one finds that the average annual number of new compounds was 2.3, 3.3, and 1.0, respectively.

A more complete measure of productivity, used in several evaluations of the pharmaceutical industry (Baily, 1972; Grabowski, Vernon, and Thomas, 1978), is R&D expenditures per new product. For the 1965-1967, 1970-1972, and 1975-1977 periods these expenditures were $13.8, $16.9, and $36.4 million, respectively. Again, there appears to be a decrease in productivity in the most recent period.

There are several possible explanations for the apparent decline in research productivity in the ani-

Table 1. Animal Drug Research and Development[a]

Year	AHI member sales ($ million)	Sales annual growth (percent)	AHI R & D ($ million)	AHI R & D deflated[b] ($ million)	Total R & D ÷ total sales	Percent of R & D innovative (percent)	New drugs approved (number)	New use registrations[d] (number)
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
1964							1	
1965	267.5		26.7	35.0	10.0		2	2
1966	300.6	12.3	31.5	40.6	10.5		4	4+1[c]
1967	322.4	7.2	38.6	48.9	11.9		3	3
1968	310.5	-3.7	41.1	49.7	13.2		6	6
1969	336.0	8.2	44.3	50.9	13.2		4	7
1970	387.9	15.4	50.7	55.2	13.1	86	5	5
1971	415.4	7.1	55.9	58.2	13.6	83	3	4
1972	459.2	10.5	55.6	55.6	12.1	81	2	2
1973	517.9	12.8	62.8	59.3	12.1	81	5	5
1974	564.8	9.0	73.4	63.1	13.0	78	0	0
1975	583.8	3.4	77.2	60.7	13.2		4	4
1976	689.9	18.2	84.3	63.1	12.2		1	1
1977	741.9	7.5	90.9	58.2	12.3	80	0	0
1978[e]	912.0	22.9					2	
Mean		9.4						

[a] From annual surveys by Ernst and Ernst for the Animal Health Institute (AHI).

[b] Column 3 divided by the GNP deflator (1972 = 100).

[c] Four separate-use compounds plus one compound with multiple uses.

[d] New entity registrations by species of animal.

[e] Preliminary data.

mal drug industry. The *depletion argument* is that over time there is a reduction of the possible stock of effective compounds so that each additional new drug becomes more and more costly to discover and develop. Baily (1972) found this effect to be important in the human drug industry. Grabowski, Vernon, and Thomas (1978) developed the method of using drug discoveries in other countries to test the level of depletion. The Animal Health Institute's observation that seven compounds available in other countries cannot be used in the United States indicates that the depletion effect may not explain the reduction in animal drug registrations in the United States. More adequate data suitable for statistical analysis are needed to test the depletion hypothesis against other explanations.

The *regulatory stringency argument* is that testing requirements for safety and efficacy approval by the Food and Drug Administration are suppressing innovative activity. The effects of regulatory stringency may take the form of delays in approval, increase in expenditures for tests, shifting of expenditures from innovative to noninnovative activities, or a combination of these. Also, threat of, or actual removal of, compounds from the market may induce reductions in innovative R&D expenditures.

There is little information on regulatory timing and expenditures for tests. Column 6 in Table 1 shows only that the share of R&D expenditures for innovative activities has declined. This may be an inaccurate measure because definitions of "innovative" activities are not fully consistent among firms and may tend to exaggerate the impact of regulations. However, it is well known that there is about a 4- to 5-year delay from adjustments in R&D to the time of submission of new compounds for FDA approval. The reductions in approvals do coincide with innovative reductions 4 to 5 years earlier (1970-73 R&D shifts and 1974-77 reductions).

Increasing testing costs can arise from both increased regulatory stringency and general price increases in performing tests. Table 2 shows the changes in costs to perform various safety tests necessary for both pesticide and animal drug registration. Note that the most precipitous increase in testing costs came not during the period of rapid inflation of 1974-1975 but rather in the 1976-1978 period. Pathologists and toxicologists are required to carry out the testing of pesticides and drugs, and training for these professions requires considerable time. The 43 percent increase in average salary of pathologists and the 23 percent increase in average salary of toxicologists between 1977 and 1979 suggests that the increased testing required has increased the demand for such specialists and the salaries they receive. Explanations of the type of regulatory actions that may induce changes in R&D investments are discussed in other sections of the report.

A *final possible reason* for decreasing animal drug innovation is that the demand for new animal drugs may have decreased. A decrease in demand for new animal drugs might reflect decreased demand for animal products, improvement in animal health, or a shift to nondrug approaches to animal health care. The recent rapid rise in the total sales value of animal health drugs (Table 1, Column 1) in the absence of drug price increases, mentioned earlier, appears to indicate a rapidly expanding market for existing drugs. Therefore, the expanding demand for drugs should be encouraging more R&D activity.

Table 2. Cost Trends per Toxicological Study and Testing Industry Wage Rates[a]

	Costs in thousands of dollars				
Year	Subchronic rat test	Chronic mouse test	Chronic rat test	Annual pathologist salary	Annual toxicologist salary
1973	10	30	50		
1974	11	35	65		
1975	12	45	72		
1976	14	55	80		
1977	20	60	120	28	22
1978	50	150	230		
1979	70	220	295	40	27

[a] Based on a survey of four private toxicological companies by Litton Bionetics. The salaries in the last two columns are for beginning, board-certified veterinary pathologists and for beginning professional toxicologists with a Ph.D. degree.

CLEARANCE OF NEW ANIMAL DRUG APPLICATIONS

The clearance procedures for new animal drugs are very complex and are poorly understood. Some procedures suggested by FDA are not explicit. This section outlines our understanding of the overall procedure involved and presents a case history of one antibiotic that was submitted for clearance in 1972 and did not receive final clearance until 1978. In addition, the regulation of essential nutrient additions to animal feeds is addressed since in many cases these also must receive FDA clearance for their use.

Figure 1 presents a flow chart which illustrates our understanding of the critical steps required in developing a new animal drug application (NADA), including the involvement of FDA. The flow chart shows the various tests required to gain approval, with time allowed for review and approval by FDA.

The actual NADA is made in triplicate on Form FD 356V (4/78), Attachment 1, and is submitted by the manufacturer to BVM as explained in the instructions on the form. Briefly, the application requires: (1) identification; (2) a table of contents and summary; (3) labeling information in detail; (4) components and composition information; (5) information on manufacturing methods, facilities, and controls; (6) samples of the new animal drug; (7) information on analytical methods for residues; (8) evidence establishing its safety and effectiveness; (9) information on compliance of new animal drugs subject to section 512 (n) of the act; (10) an environmental impact analysis; and (11) confidentiality of data in a new animal drug application.

A copy of the Internal Bureau of Foods Processing of Animal Drug Petitions, Attachment 2, explains the petition flow process within BF and how coordination is achieved with BVM. It points out how the application is logged in and how its movement is followed, along with a record of the number of days lapsed at each work station. The document also points out that, before BF can recommend approval of a new animal drug to BVM, concurrence is required from the Division of Chemistry and Physics (DCH), the Division of Toxicology (DT), and the Associate Director for Sciences (SCI). The responsibilities of each of these groups are explained in the document.

By statute, FDA is required to respond to the applicant within 180 days of submission of the NADA, informing the applicant that the application is approved or the reasons it is not approved. FDA frequently does not respond within the 180-day period; in fact, the usual response period is reported to be from about 7 months to more than 12 months. A new 180-day response period (plus any delay in responding) goes into effect each time FDA requests additional information. Thus, the time required for action can be extended 6 months or more at a time over an extended period.

Figure 2 shows a drug company's schedule for a NADA submission for clearance of a cattle feed premix, with times required to obtain the necessary data for each step in the clearance process. The study began January 15, 1975, with the final submission for NADA clearance being submitted in the second quarter of 1977. More than 2 years would be required to carry out all of the necessary tests. This example allows only a minimum of time to make all required tests and to prepare the data for submission. After the NADA has been submitted, FDA has 180 days to respond and, as already indicated, may take longer. If additional testing or information is required, FDA has an additional 180 days to respond. The requests for additional testing or information make NADA applications a "moving target" since regulations and requirements for clearance may change after the original submission; this is disconcerting to the applicant, and it discourages NADA submissions from the standpoint of both cost and uncertainty.

An actual case history with dates of submission of, and responses to, a NADA for an antibiotic to be administered in the feed is outlined in Figure 3. Four NADAs covering two dosage forms and two indications of use were submitted by the manufacturer between June 16, 1972, and July 31, 1972. BVM transmitted preliminary oral comments on all four NADAs to the manufacturer on November 30, 1972. Formal review by BVM was completed, and written comments were sent to the manufacturer, on

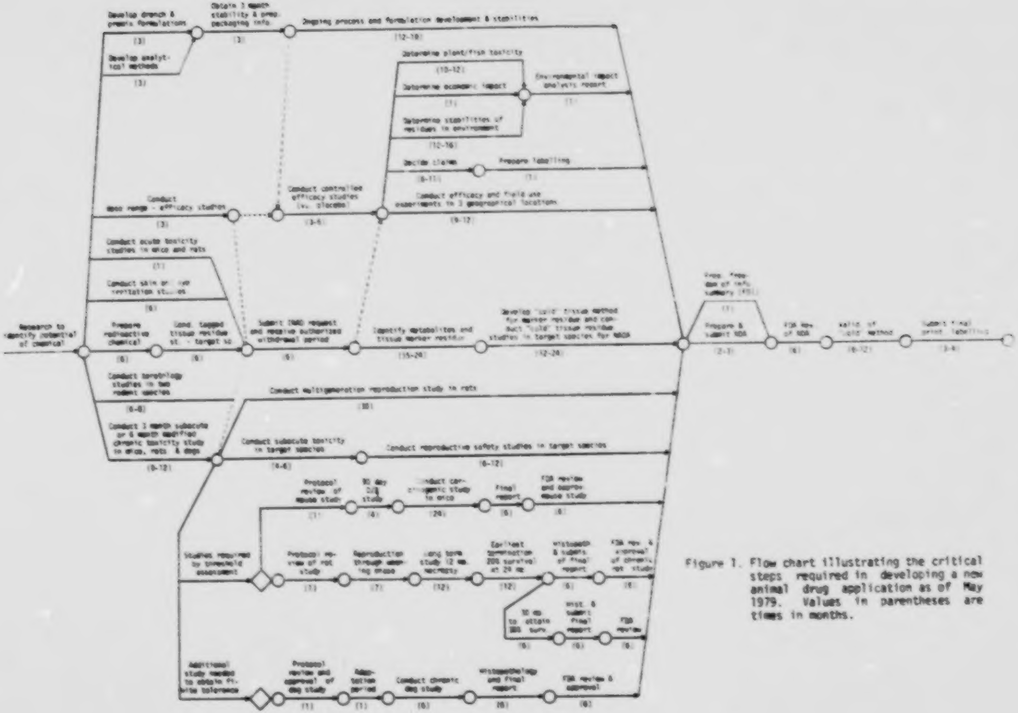
Develop drench & premix formulations
(3)
Develop analytical methods
(3)
Obtain 3 month stability & prep. packaging info.
(3)
Ongoing process and formulation development & stabilities
(12-18)
Determine plant/fish toxicity
(10-12)
Determine economic impact
(1)
Determine stabilities of residues in environment
(12-16)
Environmental impact analysis report
(1)
Decide claims
(9-11)
Prepare labelling
(1)
Conduct dose range - efficacy studies
(3)
Conduct controlled efficacy studies (vs. placebo)
(3-6)
Conduct efficacy and field use experiments in 3 geographical locations
(9-12)
Conduct acute toxicity studies in mice and rats
(1)
Conduct skin and eye irritation studies
(6)
Research to identify potential of chemical
Prepare radioactive chemical
(6)
Cond. tagged tissue residue st. - target sp
(6)
Submit INAD request and receive authorized withdrawal period
(6)
Identify metabolites and tissue marker residue
(15-20)
Develop "cold" tissue method for marker residue and conduct "cold" tissue residue studies in target species for NADA
(12-20)
Prep. freedom of info. summary (FOI)
(1)
Prepare & submit NDA
(2-3)
FDA rev. of NDA
(6)
Valid. of "cold" method
(6-12)
Submit final print. labelling
(3-4)
Conduct teratology studies in two rodent species
(6-8)
Conduct multigeneration reproduction study in rats
(30)
Conduct 3 month subacute or 6 month modified chronic toxicity study in mice, rats & dogs
(9-12)
Conduct subacute toxicity in target species
(4-6)
Conduct reproductive safety studies in target species
(6-12)
Protocol review of mouse study
(1)
90 day D/R study
(4)
Conduct carcinogenic study in mice
(24)
Final report
(6)
FDA review and approv. mouse study
(6)
Studies required by threshold assessment
Protocol review of rat study
(1)
Reproduction through weaning phase
(7)
Long term study (2 yr. necropsy
(12)
Earliest termination 20% survival at 24 mo
(12)
Histopath & submit. of final report
(6)
FDA rev. & approval of chronic rat study
(6)
30 mo. to obtain 20% surv.
(6)
Hist. & submit final report
(6)
FDA review
(6)
Additional study needed to obtain fi. nite tolerance
Protocol review and approval of dog study
(1)
Adaptation period
(1)
Conduct chronic dog study
(6)
Histopathology and final report
(6)
FDA review & approval
(6)

Figure 1. Flow chart illustrating the critical steps required in developing a new animal drug application as of May 1979. Values in parentheses are times in months.

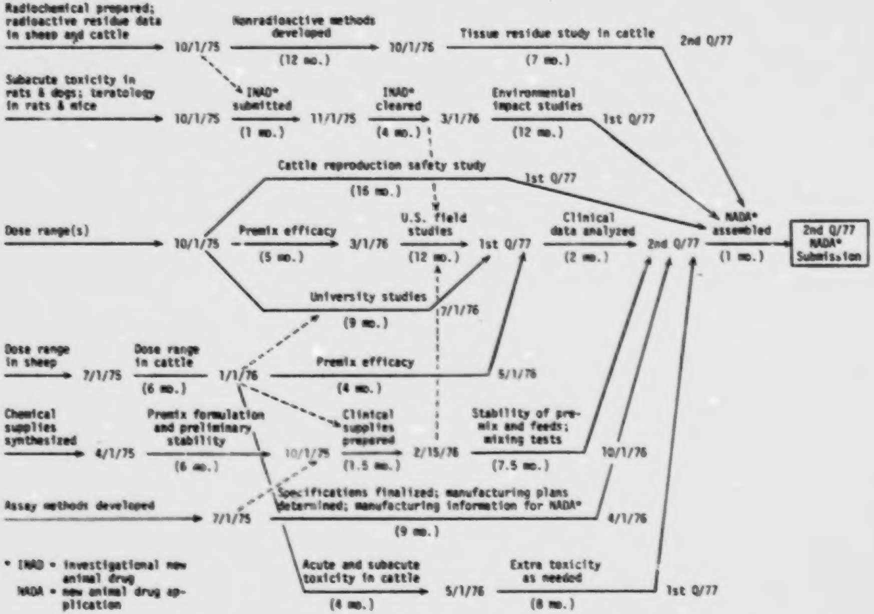
Radiochemical prepared; radioactive residue data in sheep and cattle
10/1/75
Nonradioactive methods developed
(12 mo.)
10/1/76
Tissue residue study in cattle
(7 mo.)
2nd Q/77
Subacute toxicity in rats & dogs; teratology in rats & mice
10/1/75
INAD* submitted
(1 mo.)
11/1/75
INAD* cleared
(4 mo.)
3/1/76
Environmental impact studies
(12 mo.)
1st Q/77
Cattle reproduction safety study
(16 mo.)
1st Q/77
Dose range(s)
10/1/75
Premix efficacy
(5 mo.)
3/1/76
U.S. field studies
(12 mo.)
1st Q/77
Clinical data analyzed
(2 mo.)
2nd Q/77
NADA* assembled
(1 mo.)
2nd Q/77 NADA* Submission
University studies
(9 mo.)
7/1/76
Dose range in sheep
7/1/75
Dose range in cattle
(6 mo.)
1/1/76
Premix efficacy
(4 mo.)
5/1/76
Chemical supplies synthesized
4/1/75
Premix formulation and preliminary stability
(6 mo.)
10/1/75
Clinical supplies prepared
(1.5 mo.)
2/15/76
Stability of premix and feeds; mixing tests
(7.5 mo.)
10/1/76
Assay methods developed
7/1/75
Specifications finalized; manufacturing plans determined; manufacturing information for NADA*
(9 mo.)
4/1/76
Acute and subacute toxicity in cattle
(4 mo.)
5/1/76
Extra toxicity as needed
(8 mo.)
1st Q/77
* INAD = investigational new animal drug
NADA = new animal drug application

Figure 2. A drug manufacturer's plan of action with estimated times for obtaining and processing various parts of the information required to obtain approval from the Food and Drug Administration for sale of the dosage form (premix) of an anthelmintic drug for cattle. The premix is intended for sale to feed manufacturers.

Figure 3. A Chronology of the Submission and Review of New Animal Drug Applications for an Antibiotic Proposed for Use in Animal Feeds at Two Levels of Dosage and With Two Indications of Use

1.	Four NADAs covering two dosage forms and two indications of use were initially submitted by the manufacturer	6/16/72 6/19/72 7/28/72 7/31/72
2.	Preliminary oral comments were received by the manufacturer from BVM concerning all NADAs submitted	11/30/72
3.	Formal review by BVM was completed, and final additional comments from BVM were received by letter by the manufacturer	2/06/73
4.	Manufacturer submitted a reply to FDA answering questions raised as the result of the 2/6/73 review	3/01/73
5.	BVM advised the manufacturer that a range of doses for one of the claims would not be acceptable	4/10/73
6.	Manufacturer withdrew claim for the range of doses and submitted a request for one dose level	4/12/73
7.	Review of original submissions and all amendments submitted through 4/12/73 was completed, and additional comments were received from BVM by the manufacturer	6/11/73
8.	BVM requested that the four NADAs be consolidated into two NADAs	7/22/74
9.	BVM advised that the two NADAs were approvable and requested final printed labeling	9/19/74
10.	Final printed labeling was submitted by the manufacturer	9/27/74
11.	Federal Register notice approving NADAs was published	12/17/74
12.	Supplemental NADA providing for use of product to market weight was submitted to BVM by the manufacturer	7/14/75
13.	Reply received by the manufacturer from BVM advising that until additional safety data were received and reviewed no comments would be forthcoming and the application was considered withdrawn	7/31/75
14.	Manufacturer resubmitted supplemental application to BVM requesting extension of claims to market weight	1/28/76
15.	Manufacturer received letter from FDA notifying that BF had completed review of safety data and that there was no objection to extension of the claim to market weight	7/27/76
16.	Label revisions, Environmental Impact Analysis Report, and Freedom of Information Summary consistent with guidelines effective July 31, 1976, were requested by BVM	10/27/76
17.	Manufacturer hand-delivered revised Freedom of Information Summary, Environmental Impact Analysis Report, and final printed labeling and packaging information to BVM	11/24/76
18.	BVM advised the manufacturer that BF scientists had decided to modify data requirements for this class of drugs to establish adequately the conditions of safe use	1/31/77
19.	Manufacturer forwarded a request to BVM for approval of supplementary applications with a commitment on the part of the manufacturer to complete the modified requirements	2/09/77
20.	BVM advised the manufacturer that data requirements considered necessary to affirm safe use must be met prior to approval, since the supplemental applications constituted a risk of increased human exposure	2/18/77
21.	Manufacturer submitted required additional safety data, revised Freedom of Information Summary, and amended Environmental Impact Analysis Report	1/24/78
22.	FDA requested more detail in Freedom of Information Summary	3/01/78
23.	Manufacturer submitted revised Freedom of Information Summary	3/28/78
24.	Manufacturer met with FDA officials to review questions regarding additional safety data submitted	3/30/78
25.	Review was completed; request for final labeling was received by the manufacturer	8/02/78
26.	Manufacturer submitted final labeling	8/14/78
27.	Federal Register notice of supplemental clearance was published by FDA	9/19/78

February 6, 1973. The response time varied from 190 days for the last NADA submitted to 235 days for the earliest one.

On March 1, 1973, the manufacturer replied to questions raised by BVP. BVM promptly advised the manufacturer on April 10, 1973, that the range of dosages prescribed in one of the claims was not acceptable. On April 12, 1973, the manufacturer withdrew the claim on a range of dosages and submitted a request for a single dose level.

BVM reviewed the original submissions and all amendments previously submitted by the manufacturer and, on June 11, 1973, sent additional comments to the manufacturer. On July 22, 1974--over a year later--BVM requested that the four NADAs be consolidated into two NADAs. The manufacturer complied with the request. On September 19, 1974, BVM advised the manufacturer that the two NADAs were approvable and requested final printed labeling, which was submitted on September 27, 1974. Then on December 17, 1974, a notice of approval of the two NADAs was published in the *Federal Register*.

BVM then asked for verification of the usefulness of the product in feeding animals to market weight. Verification was supplied by the manufacturer on July 14, 1975. On July 31, 1975, BVM advised the manufacturer that additional safety data were needed and that until they were received and reviewed, the application would be considered withdrawn.

The manufacturer obtained supporting data for the safety of the antibiotic and resubmitted a supplemental application to BVM on January 28, 1976, requesting extension of claims to market weight. On July 27, 1976, the manufacturer received a letter from FDA indicating that BF had completed a review of the safety data and concluded that there was no objection to extension of the claim for the use of the product to market weight. On October 27, 1976, BVM requested label revisions, an Environmental Impact Analysis Report, and a Freedom of Information Summary consistent with the guidelines for July 31, 1976. These documents were hand-delivered to BVM on November 24, 1976.

On January 31, 1977, the manufacturer received a reply from BVM stating that BF scientists had decided to modify the data requirements for this class of drugs to establish more adequately the conditions for safe use. The manufacturer forwarded a request to BVM on February 9, 1977, for approval of supplementary applications with a commitment on the part of the manufacturer to complete the modified requirements. A reply from BVM was received by the manufacturer February 18, 1977, stating that the data requirements showing the product to be safe must be submitted prior to approval for supplementary use, since the supplemental applications constituted a risk of increased human exposure.

The manufacturer submitted the required additional safety data, a revised Freedom of Information Summary, and an amended Environmental Impact Analysis Report on January 24, 1976. On March 1, 1978, FDA requested more details in the Freedom of Information Summary; these were submitted by the manufacturer on March 28, 1978.

On March 30, 1978, representatives of the manufacturer met with FDA officials and reviewed questions on the additional safety data submitted. The FDA review was completed and a request for final labeling was received by the manufacturer on August 2, 1978. Final labeling was submitted to FDA on August 14, 1978. On September 19, 1978, a notice of supplemental clearance for broad usage of the antibiotic was published in the *Federal Register*.

The chronology of the review process outlined in Figure 3 points out the difficulties encountered in obtaining clearance of one antibiotic. Although two of four original NADAs were approved in 2 years and 4 to 5 months from the original submission dates, this was only for limited usage. An additional 3 years and 2 months were required to obtain clearance for broad usage of the product. The step-by-step documentation outlined herein clearly illustrates that the approval process for new animal drugs is slow, confusing, and frustrating. In spite of the voluminous amount of data and information required in the original NADA, the clearance procedure required a great deal of additional supporting information before approval. FDA seemingly considered only one step at a time instead of indicating in one communication all the points on which added information or data were needed.

The process of approving new animal drugs could be accelerated and made more efficient if the information to be required were clearly specified in writing at the beginning of the process and if some allowance were made for the changes in requirements that are introduced after the manufacturer has committed resources to obtaining the information specified initially. Changes in requirements may result, not only from new developments in regulations, but also from differences in interpretations and personal views as new FDA personnel become involved in the approval process.

REGULATION OF ESSENTIAL NUTRIENT ADDITIONS TO ANIMAL DIETS

Essential nutrients are substances which must be present in the diet of an animal because they cannot be synthesized by the animal's own tissues or, in ruminants, by microbial symbionts in the gastrointestinal tract. When these nutrients are missing from the diet or are present in less than required amounts, animal health is adversely affected. This illness may be expressed in a variety of ways, depending upon the function of the nutrient and the degree of its deficiency. Sometimes a marginal deficiency may be detected only by examining the activity of certain blood enzymes or by determining the concentration of the nutrient in certain tissues. There may be no clinical signs; and only when a secondary stressor, such as inclement weather, is superimposed, is the deficiency overtly expressed. Some nutrient deficiencies result in skin lesions, impaired locomotion, diminished vision, or nerve dysfunction. Growth may slow, and reproduction may cease. The ultimate deficiency sign is death.

The essentiality of a substance as a nutrient and the amount of an essential nutrient required are natural phenomena. The phenomena can be elucidated by experimentation, but they are not subject to human laws or regulations.

The Federal Food, Drug and Cosmetic Act, as amended (Food and Drug Administration, 1979a), does not include a definition of essential nutrients for animals. The term "animal feed" has been interpreted by FDA to include this class of substances, and the official position of BVM relative to regulation of nutrients in animal feeds was outlined in the BVM Policy and Procedures Manual published in 1976. While many of these regulations appear reasonable in intent, they are couched in terms that allow arbitrary application. For example, one section reads "Vitamins and minerals may be present in premixes intended for use in non-medicated animal feed, and in animal feed itself provided . . . there is an established need for each nutrient in the target animal; that it is present at levels consistent with recognized nutritional needs in a stable and biologically available form; that recognized safe levels are not exceeded unless otherwise cleared; and that the feed is not otherwise adulterated or misbranded." Established need has generally been based on definition of quantitative requirements for the target animal by the Committee on Animal Nutrition (CAN) of the National Academy of Sciences - National Research Council. Since quantitative nutrient requirements are not usually defined by CAN unless published scientific data are considered adequate, the BVM staff has the option of concluding that, in the absence of a quantitative nutrient requirement set by CAN, there is no established need, despite clear evidence of a qualitative requirement.

An additional complication is introduced by interactions of nutrients that modify quantitative requirements, *e.g.*, the well-known increase in the need for zinc in the diet of swine when dietary calcium concentrations are increased. Such interactions demand flexibility in the levels of nutrients permitted in diets so that they can be truly "in accordance with good manufacturing or feeding practice," as stated in the Code of Federal Regulations for general purpose food additives (21 CFR § 582.1005 et seq.).

Other environmental factors also may modify the need for supplemental nutrients. Moldy corn fed to swine sometimes contains antivitamin K substances which result in fatal hemorrhages in young pigs at the time of castration. Supplemental vitamin K will prevent the problem, but CAN has only recently established a quantitative requirement for this nutrient, and strict interpretation of BVM regulations would deter addition of vitamin K to the feed.

Since essential nutrient additions to animal diets are regulated as food additives or through qualification for the generally recognized as safe (GRAS) list, individuals who wish to fortify animal diets with nutrients recently recognized (since 1958) as essential must file a petition with FDA, proposing issuance of a regulation prescribing the conditions under which such additives may be safely used. Since essential nutrients are not optional additives to diets which are demonstrably deficient, restrictions on their use pose a dilemma. If essential nutrients are not added to animal diets which are known to be deficient, illness and death may be expected. If unapproved nutrients are added to such diets, one may be in violation of FDA regulations.

To gain FDA approval of nutrient additions is not a simple matter. Nutrients are seldom in proprietary form, and individual companies are loathe to make the financial commitment necessary to gain FDA approval for their use. This problem has caused difficulties as animal production systems have changed, leading to deficiencies of certain nutrients--such as selenium--which previously were of little concern.

Selenium was established as an essential nutrient in 1957, and extensive areas of the United States have been determined to be selenium-deficient. Since the amount of selenium needed in the diet tends to be inversely related to vitamin E intake, the use of pasture (normally containing high concentrations of vitamin E), or of other high vitamin E feeds, masked all but the more severe selenium deficiencies. However, dramatic reductions in the use of pasture for livestock have taken place over the past 20 years, markedly decreasing vitamin E consumption. Feeds for chickens, turkeys, and swine contain fewer ingredients that supply vitamin E from natural sources than they did earlier. As a consequence, selenium-vitamin E deficiency has increased.

United States Department of Agriculture (USDA) statistical summaries for 1970 indicated that approximately 65 percent of the laying hens, 55 percent of the broilers, and 50 percent of the turkeys were produced in selenium-deficient states. Economic losses to poultry producers associated with lack of approval for addition of inorganic selenium to poultry diets were calculated by FDA staff members to be in excess of $27 million annually (Food and Drug Administration, 1974). Selenium deficiency was calculated to be causing annual losses of about $55 million to the swine industry.

The first petition to FDA for GRAS status for selenium was filed in 1970 (see Attachment 3). GRAS status was denied. Petitions for food additive approval were then filed. After many man-years of research by agricultural experiment station scientists, approval for selenium as a food additive was granted in 1974. In the meantime, economic losses in the swine and poultry industry had accumulated to an estimated $328 million.

Previously, white muscle disease (selenium-vitamin E deficiency) had been diagnosed in lambs and calves in 30 of the 50 states (Wolf et al., 1963). Despite the discovery in 1958 that selenium would protect against this disease in young ruminants, it was still not legal to supplement deficient ruminant diets in 1975. USDA agricultural statistics for that year showed that approximately 51 percent of the beef cattle, 69 percent of the dairy cattle, and 31 percent of the sheep were produced in selenium-deficient states. Total losses from selenium-vitamin E deficiency during 1975 to producers of these three species were estimated to be nearly $545 million (Selenium for Ruminants Task Force, 1976).

In 1975 a Selenium for Ruminants Task Force, involving scientists from nine universities, was formed specifically to gather information which might satisfy the regulatory requirements of FDA. On January 29, 1979, approval for supplementing ruminant diets with selenium was granted.

Twenty-two years have passed since the essential nature of selenium was discovered. This period includes 12 years during which the efforts of large numbers of scientists were directed specifically toward gaining FDA approval for selenium supplements to food animal diets. This task is still not complete, since FDA has not approved selenium supplements for hens producing eggs for human consumption. This omission is not based on concern for human health since the literature (Arnold et al., 1972, 1973; Cantor and Scott, 1974; Combs and Scott, 1977; Latshaw, 1975; Ort and Latshaw, 1978; Thapar et al., 1969) contains adequate evidence of the safety of the practice. Rather, approval has not been granted because an appropriate petition has not yet passed through the regulatory protocol. The research costs related to meeting regulatory requirements for selenium cannot be precisely estimated. The specific projects involving the Selenium for Ruminants Task Force were budgeted at $173,124 for a 1-year period. It would be conservative to suggest that the effort expended so far in meeting regulatory requirements for selenium has cost over a million dollars. The inability to supplement demonstrably deficient diets during this period has cost hundreds of millions.

PROSPECTS FOR REGULATORY CHANGE IN ANIMAL DRUGS AND NUTRIENTS

The food and drug laws in the United States have undergone considerable change since 1906. A number of persons are now advocating that the time is ripe for changes in regulations to avoid stagnation of research on new drugs, to ease the burden and costs of regulation, and to focus on issues of safety in the food supply. For example, the Scientific Committee, Food Safety Council (1978), has published a proposed "System for Food Safety Assessment." The proposed system regards a substance as safe if it presents a socially acceptable risk of an unfavorable effect at levels of consumption that are experienced by high consumers of food in which the substance occurs.

Clearance for the use of a chemical substance in animal feeds requires that a food additive petition be filed unless the substance in question can be generally regarded as safe (GRAS). For a substance to be approved as GRAS, its safety must be well documented in the scientific literature. Approval of a petition for use of a chemical substance as a food additive requires documentation as to its safety and efficacy, but it need not be documented in the scientific literature. In some instances, it appears to be easier to obtain approval as a food additive than it is to gain approval as GRAS.

A clear and distinct protocol for submitting and approving requests for both GRAS and food additives would assist the industry in obtaining approvals and would also reduce its criticism of the regulations. It could also reduce the regulatory burden connected with reviewing and approving petitions.

Several recent documents indicate the existence of concern within FDA for the problems of regulating animal drugs. The first such document is the report and recommendations of the Medicated Feed Task Force entitled "Second Generation of Medicated Feeds." This internal document recommends orienting the medicated feed program to maximize public health protection. Questions of animal safety and drug efficacy would be less important to regulation while human health risk potential would become the key issue according to the recommendations in the report. The authors conclude that human safety is the proper departure point for determining whether a drug used in animal feed is a "new animal drug" and therefore subject to rigorous control under FFDCA. This approach would probably be accepted by most persons.

Many problems exist with the current medicated feed program. Those cited in the FDA report include: (1) regulations do not effectively focus on problems related to human health, (2) administration of the current program generates unnecessary paper work and expends staff time without relevance to public health protection, (3) good manufacturing practices are not assured since many applications for drug use are made by drug companies for feed manufacturers who do not have adequate equipment to prepare feeds from concentrated drug premixes, (4) obligations to inspect the large number of medicated feed firms cannot be met or carried out adequately due to lack of resources and due to lack of guidance and training of FDA field staff and cooperating state personnel, and (5) violations are not adequately dealt with under current regulation.

If the recommendations of the Medicated Feed Task Force were adopted and implemented, regulations would concentrate on preventing harmful drug residues from being introduced into the human food supply. Under the proposal, all drugs would be classified according to the degree of risk they present to humans from drug residues in food. A system for classifying drugs into risk categories is proposed in the document. Where there is no risk or the risk is very small, the drug would not be subject to regulatory control. Where the risk of residues is potentially significant, as in the case of carcinogens, approval of medicated feed applications by FDA would contribute to proper use of the drug in feeds. In this way, FDA resources at the preclearance level could be used more effectively to maximize human health protection. The surveillance and compliance aspects of the program would also be directed to those drugs for which the risk of residues is potentially significant to human health.

The Medicated Feed Task Force estimates that implementation of the recommendations would eventually result in 50 percent fewer submissions of Medicated Feed Applications (Form FD-1800). In addition, the Task Force recommends that new drug applications be simplified with emphasis on label reviews; that feed mill inspections be limited to firms requiring new drug approvals; that the state contract program for regulation of medicated feeds be revitalized; and that a comprehensive training program be established for FDA and state personnel involved in the new regulatory program.

The second document, containing proposed rules on "Criteria and Procedures for Evaluating Assays for Carcinogenic Residues in Food-Producing Animals," was published in the *Federal Register*, volume 44, number 55, pages 17070 to 17114, Tuesday, March 20, 1979. This proposal would set requirements for safety testing of animal drugs, food additives, and color additives and for analytical methods to detect residues of these substances in meat, milk, and eggs. Since each method has a limit to its sensitivity, no method can ascertain absolutely that no residue is present. Hence, rules are proposed in this sensitivity of method (SOM) document to ensure that any residues escaping detection by an approved method do not pose a significant risk of cancer to humans. "No significant risk" is defined as a level of residue that would have [illegible] probability of causing no more than one cancer in [illegible] million lifetimes.

An examination by FDA of the effect of the SOM threshold assessment scoring system on currently approved drugs would be of value to all concerned as a basis for perspective. The SOM appears to broaden the process of drug approval and to bring within purview many compounds that are unlikely to have carcinogenic potential. A threshold procedure that does not discriminate between compounds that merit extensive testing and those that do not would result in misallocation of scientific resources and would deter development of useful animal drugs of limited market potential. In addition, the "use factor" proposed as a part of the scoring system focuses on the number of animals potentially treated rather than on the amount of edible tissue consumed. (Each American annually consumes, on the average, about 17 chickens and 20 percent of a beef carcass, but the carcass weights involved are about 48 and 120 pounds, respectively.)

The SOM also proposes that residue limits be based on concentrations in the "edible tissue that is the most efficient accumulator of residues." Since kidney and liver are frequently the "most efficient accumulators" but are consumed in much smaller amounts than muscle, this proposal does not realistically deal with potential human exposure.

Another reservation concerning the SOM document is that it proposes to estimate potential carcinogenicity by linear extrapolation from doses observed to be carcinogenic to zero. There is serious doubt that the linear extrapolation model and the one-hit theory of carcinogenesis involved in this extrapolation are appropriate for all compounds, particularly those that are normally produced in the body.

To restrict drug evaluation to the rigid system proposed would be valuable in the sense that everyone would know what was involved and could proceed accordingly. On the other hand, the system proposed is not now scientifically validated, and its adoption as a regulation would have the effect of inhibiting scientific advances and of directing scientific work along lines that may eventually be found inappropriate.

Moreover, it is a violation of statistical principles to deny that a single animal might occasionally fall beyond the ninety-ninth percentile relative to residues of substances normally produced in the body. For such animals to be judged in violation of federal regulation would be inconsistent with the statistical principle that, in a population of animals, one animal in 100 would normally be expected to fall in this position. This violation of statistical principles is not ameliorated by the requirement that 450 to 500 animals be used in each experimental group (p. 17098). Such a requirement would be extremely difficult to comply with if the target animals were cattle.

Problems associated with clearance of drugs of limited use (minor drugs or use of drugs for minor species) are apparently receiving some consideration by FDA. A major problem here is that there is too little economic incentive for companies to clear drugs for use when the potential market for them is restricted to a small volume because they are not frequently used or their use is for a minor species of animal, such as rabbits, ducks, or sheep. In such cases, the investment in providing required preclearance information on the drug may exceed projected profits from the sale of the drug. Satisfactory rules and regulations are needed for these situations in which the drugs are of significant value to agricultural producers even if those producers are limited in number. One possibility is for a reduction in requirements for preclearance of major drugs for minor species.

Recently a third document entitled "Safety and Effectiveness Data Supporting the Approval of Minor Use New Animal Drugs" was published in the *Federal Register*, part 3, for Friday, July 20, 1979. This proposal speaks to rule changes that would make it possible to extrapolate data from one species to another species in the support of applications for the use of new drugs in minor species of animals. Adoption of this proposal would probably stimulate drug applications for use in minor species where they are now absent.

Another possibility is the adoption of a "temporary clearance" device to permit the use of animal health and nutrient chemicals after preliminary data appear promising but before the bank of data required for the present permanent "clearance" has been fully accumulated and approved. After further experience, including monitoring, such a product could then be given regular clearance if no adverse affects are observed. If problems occur, the temporary clearance could be revoked without any new authority. This procedure would greatly speed the process of approval and would increase the availability of drugs and other feed additives for use in minor species.

One of the problems in the minor species area is the fact that a species classed as minor from a drug-use standpoint may be classified as major by FSQS; sheep are a case in point. Thus, although BVM might relax its testing requirements for new chemicals, FSQS and BF consider sheep a major species and are as inflexible in their residue requirements as they are for a major drug-use species. This viewpoint is justified on the basis that sheep are a part of the food supply. Thus, an attempt to make it easier to obtain approval of chemicals for a minor species could conceivably be no advantage at all, and in some instances could actually lead to additional problems.

Clearance of a minor drug for a major species is another matter. In this case, the most feasible way to expedite clearance appears to be to accept less rigorous pretesting requirements. Whether or not adequate pretesting could be done with scaled-down requirements probably would require scientific judgment. For each compound that might potentially be involved, data concerning toxicity, carcinogenicity, teratogenicity, etc. would need to be considered.

It seems unlikely that ways will be found to stimulate drug clearance applications from manufacturers for use of minor drugs in minor species. This last case might best be handled by a combination of one of the possibilities mentioned previously with sponsorship of the costs of preclearance testing by a government agency, state experiment station, or agricultural industry organization. FDA has not yet published proposals to deal with the minor drug, minor species problem.

Obtaining clearance for nonpatented or nonproprietary products is another major problem. Because all companies can sell them, there is insufficient incentive for any one company to undertake the expense required to obtain clearance. As a consequence, such products are almost eliminated from the market. A similar situation prevails with products on which the patents have expired. Many such former proprietary products with a long history of usefulness are discontinued because there is insufficient economic incentive for any one company to carry out the additional research needed to obtain clearance on the basis of current data requirements. This seeming dilemma and the societal loss it entails might be resolved by a combination of change in data requirements with a means to provide certain protection for companies that invested the resources needed to clear the products.

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ATTACHMENT 1
NEW ANIMAL DRUG APPLICATION

Form FD 356V (4/78)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION **NEW ANIMAL DRUG APPLICATION** *(Drugs for Animal Use)* *(Title 21, CFR § 514)*	**FOR FDA USE ONLY** NADA NO. DATE RECEIVED

NAME OF APPLICANT		TYPE OF SUBMISSION *(Check one)* ☐ ORIGINAL APPLICATION *(CFR 514.1(a))* ☐ AMENDMENT TO AN UNAPPROVED ORIGINAL APPLICATION *(CFR 514.6)* ☐ AMENDMENT TO AN UNAPPROVED SUPPLEMENT TO AN APPROVED APPLICATION *(CFR 514.6)* ☐ SUPPLEMENT TO AN APPROVED APPLICATION *(CFR 514.8 (a))* ☐ SPECIAL NEW ANIMAL DRUG APPLICATION SUPPLEMENT - CHANGES BEING EFFECTED *(CFR 514.8 (a))*
ADDRESS *(Street Number, City, and Zip Code)*		
FDA DRUG REGISTRATION NO.	DATE	

CHEMICAL NAME *(In cases of multi-component drug mixtures a continuation sheet must be attached)*	GENERIC NAME PROPRIETARY NAME

INSTRUCTIONS FOR PREPARING AND SUBMITTING THE NEW ANIMAL DRUG APPLICATION

i. Assemble and bind three identical copies of the submission.

ii. Identify each front cover with the name of the applicant, the proprietary name, if available, the name of the new animal drug and the dosage form.

iii. Use separate pages for each numbered heading consistent with subparagraph (1) through (11) of this Application form. Number the pages of the new animal drug application. Each copy should bear the same page numbering.

iv. Each copy of an original new animal drug application shall contain three complete sets of labeling.

v. Submit separate applications for each different dosage form of the drug proposed. Repeating in each application basic information pertinent to all dosage forms is unnecessary if reference is made to the application containing such information. Such references should be made by volume and page. Include in each application information applicable to the specific dosage form, such as labeling, composition, stability data, efficacy data, method of manufacture and investigational new animal drug application number.

vi. Forward amendments, supplements, reports and other correspondence submitted after the original application in the above format. Identify the submission with the assigned NADA number. If the submission is a supplemental application, full information shall be provided on each proposed change concerning any statement made in the approved application.

vii. Submit to:

Food and Drug Administration
Bureau of Veterinary Medicine *(HFV-16)*
5600 Fishers Lane
Rockville, MD 20857

The undersigned submits this application for a new animal drug pursuant to section 512(b) of the Federal Food, Drug, and Cosmetic Act. It is understood that the labeling and advertising for the new animal drug will prescribe, recommend, or suggest its use only under the conditions stated in the labeling which is part of this application and if the article is a prescription new animal drug, it is understood that any labeling which furnishes or purports to furnish information for use or which prescribes, recommends, or suggests a dosage for use of the new animal drug will also contain, in the same language and emphasis, information for its use including indications, effects, dosages, routes, methods, and frequency and duration of administration, any relevant hazards, contraindications, side effects, and precautions contained in the labeling which is part of this application in accordance with 21 CFR 201.105. It is understood that all representations in this application apply to the drug produced until changes are made in conformity with § 514.8. It is further understood that new animal drugs as defined in § 510.3, intended for use in the manufacture of animal feeds in any State will be shipped only to persons who may receive such drugs in accordance with § 510.7. The undersigned certifies, that the methods, facilities, and controls described under item 5 of this application conform to the current good manufacturing practice regulations in 21 CFR PART 200.

No new animal drug application may be processed unless a completed application form has been received (21 CFR 514.1).

SIGNATURE OF APPLICANT *(Responsible offical or Authorized Agent)*	TITLE OF AUTHORITY	DATE SUBMITTED

NOTE: This application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of and must be countersigned by an authorized attorney, agent, or official residing or maintaining a place of business within the United States.

(Warning: A willfully false statement is a criminal offense. U.S.C. Title 18, sec. 1001)

Enter the estimated time (manhours) to prepare this application. *(Include typing, photocopy and assembly only)*	Original Copy	
	Duplicate/Triplicate Copies	
	TOTAL (manhours)	

FORM FD 356V (4/78) PREVIOUS EDITIONS ARE OBSOLETE *Form Approved: OMB No. 57-R0082*

The following information, described in 21 CFR 514, shall constitute the requirements of this application:

1. **Identification.** Whether the submission is an original or supplemental application; the name and address of the applicant; the date of the application; the trade name(s) (if one has been proposed) and chemical name(s) of the new animal drug. Upon receipt, the application will be assigned an NADA number, which shall be used for all correspondence with respect to the application.

2. **Table of Contents and Summary.** The application shall be organized in a cohesive fashion, shall contain a table of contents which identifies the data and other material submitted, and shall contain a well organized summary and evaluation of the data in the following form
   - *i.* Chemistry
     - *a.* Chemical structural formula or description for any new animal drug substance.
     - *b.* Relationship to other chemically or pharmacologically related drugs.
     - *c.* Description of dosage form and quantitative composition.
   - *ii.* Scientific rationale and purpose the new animal drug is to serve
     - *a.* Clinical purpose.
     - *b.* Highlights of laboratory studies. The reasons why certain types of studies were done or omitted as related to the proposed conditions of use and to information already known about this class of compounds. Emphasize any unusual particularly significant pharmacological effects or toxicological findings.
     - *c.* Highlights of clinical studies. The rationale of the clinical study plan showing why types of studies were done, amended, or omitted as related to laboratory studies and prior clinical experience.
     - *d.* Conclusions. A short statement of conclusions combining the major points of effectiveness and safety as they relate to the use of the new animal drug.
     - *e.* List of references. References to pertinent information including information contained in files of the Food and Drug Administration as provided in 21 CFR 511.1.

3. **Labeling.** Three copies of each piece of all labeling to be used for the article (total of 9).
   - *i.* All labeling should be identified to show its position on, or the manner in which it is to accompany the market package.
   - *ii.* Labeling for nonprescription new animal drugs should include adequate directions for use by the layman under all conditions of use for which the new animal drug is intended, recommended, or suggested in any of the labeling or advertising sponsored by the applicant.
   - *iii.* Labeling for prescription veterinary drugs should bear adequate information for use under which veterinarians can use the new animal drug safely and for the purposes for which it is intended, including those purposes for which it is to be advertised or represented, in accord with 21 CFR 201.105.
   - *iv.* All labeling for prescription or nonprescription new animal drugs shall be submitted with any necessary use restrictions prominently and conspicuously displayed.
   - *v.* Labeling for new animal drugs intended for use in the manufacture of medicated feeds shall include:
     - *a.* Specimens of labeling to be used for such new animal drug with adequate directions for the manufacture and use of finished feeds for all conditions for which the new animal drug is intended, recommended, or suggested in any of the labeling, including advertising, sponsored by the applicant.
     - *b.* Specimens of all labeling representative of those proposed to be used for finished feeds manufactured from the new animal drug.
   - *vi.* Draft labeling may be submitted for preliminary consideration of an application. Final printed labeling will ordinarily be required prior to approval of an application. Proposed advertising for veterinary prescription drugs may be submitted for comment or approval.

4. **Components and Composition.** A complete list of all articles used for production of the new animal drug including a full list of the composition of each article.
   - *i.* A full list of the articles used as components of the new animal drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new animal drug and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each component should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary name is used it should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed component may be specified.
   - *ii.* A full statement of the composition of the new animal drug. The statement shall set forth the name and amount of each ingredient whether active or not, contained in a stated quantity of the new animal drug in the form in which it is to be distributed (for example, amount per tablet or milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variation may be specified.
   - *iii.* If it is a new animal drug produced by fermentation:
     - *a.* Source and type of microorganism used to produce the new animal drug.
     - *b.* Composition of media used to produce the new animal drug.
     - *c.* Type of precursor used, if any, to guide or enhance production of the antibiotic during fermentation.
     - *d.* Name and composition of preservative, if any, used in the broth.
     - *e.* A complete description of the extraction and purification processes including the names and compositions of the solvents, precipitants, ion exchange resins, emulsifiers, and all other agents used.
     - *f.* If the new animal drug is produced by a catalytic hydrogenation process (such as tetracycline from chlortetracycline) a complete description of each chemical reaction with graphic formulas used to produce the new animal drug, including the names of the catalyst used, how it is removed, and how the new animal drug is extracted and purified.

5. **Manufacturing Methods, Facilities, and Controls.** A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the new animal drug. This description should include full information with respect to any new animal drug in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing, and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the new animal drug, and the following:
   - *i.* If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new animal drug, he shall: Identify each person who will perform any part of such operations and designate the part; and provide a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls he will use in his part of the operation. The statement shall include a commitment that no change will be made without prior approval by the Food and Drug Administration, unless permitted under 21 CFR 514.8.
   - *ii.* A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the new animal drug has the identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.
   - *iii.* A description of the physical facilities, including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.
   - *iv.* The methods used in the synthesis, extraction, isolation, or purification of any new animal drug. When the specifications and controls applied to such new animal drugs are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperature, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the new animal drug may be specified. A flow sheet and indicated equations should be submitted when needed to explain the process.
   - *v.* Precautions to insure proper identity, strength, quality, and purity of the raw materials, whether active or not, including:
     - *a.* The specifications for acceptance and methods of testing for each lot of raw material.
     - *b.* A statement as to whether or not each lot of raw material is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.
   - *vi.* The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new animal drug, including:
     - *a.* The method of preparation of the master formula records and individual batch records and the manner in which these records are used.
     - *b.* The number of individuals checking weight or volume of each individual ingredient entering into each batch of the new animal drug.
     - *c.* A statement as to whether or not the total weight or volume of

each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

d. The precautions used in checking the actual package yield produced from a batch of the new animal drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

e. The precautions used to assure that each lot of the new animal drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

f. Any special precautions used in the operations.

vii. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the new animal drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components.

a. A description of practicable methods of analysis of adequate sensitivity to determine the amount of the new animal drug in its final dosage form including finished feeds and in drinking water should also be included. Methods should be included for any premix or other intermediate mix for such drugs. Where two or more active ingredients are included, methods should be quantitative and specific for each active ingredient.

b. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

viii. An explanation of the exact significance of any batch control numbers used in the manufacturing, processing, packaging, and labeling of the new animal drug, including such control numbers that may appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

ix. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

x. A complete description of, and data derived from, studies of the stability of the new animal drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies underway or planned. Stability data should be submitted for any new animal drug, for the finished dosage form of the new animal drug in the container in which it is to be marketed, including any proposed multiple-dose container, and, if it is to be put into solution at the time of dispensing, for the solution prepared as directed. If the data indicate that an expiration date is needed to preserve the identity, strength, quality, and purity of the new animal drug until it is used, the applicant shall propose such expiration date. If no expiration date is proposed the applicant must justify its absence.

xi. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product. An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the new animal drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.

xii. The methods, facilities, and controls described under item 5 of this application conform to the current good manufacturing practice regulations in 21 CFR 200.

xiii. An analysis of the environmental impact of the manufacturing process(es) of the article that is the subject of the requested action as specified under 21 CFR 25.1(g).

Include

(1) An identification of pollutants expected to be emitted.

(2) A citation of applicable Federal, state, and local emission requirements, and,

(3) A certification that such emission complies with said requirements. Where there are no applicable Federal, state or local emission requirements, citation and certification shall be made to appropriate industry, advisory, or voluntary standards acceptable to the agency.

6. **Samples.** Samples of the new animal drug and articles used as components and information concerning them may be requested by the Bureau of Veterinary Medicine as follows:

i. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new animal drug application to which it relates. Included are:

a. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new animal drug and other assayed components of the finished new animal drug.

b. A representative sample or samples of each strength of the finished dosage form proposed in the application and employed in the clinical investigations and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form.

c. A representative sample or samples of finished market packages of each strength of the dosage form of the new animal drug prepared for initial marketing and, if any such sample is not from a representative commercial-scale production batch, such a sample from a representative commercial-scale production batch, and a representative sample or samples of each new animal drug from the batch(es) employed in the production of such dosage form, provided that in the case of new animal drugs marketed in large packages the sample should contain only three times a sufficient quantity of the new animal drug to allow for performing the control tests for drug identity and assays.

ii. The following information shall be included for the samples when requested:

a. For each sample submitted, full information regarding its identity and the origin of any new animal drug contained therein (including a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays.

b. For any reference standard submitted, a complete description of its preparation and the results of all laboratory tests on it, if the test methods used differed from those described in the application, full details of the methods employed in obtaining the reporting results.

7. **Analytical Methods for Residues.** Applications for new animal drugs shall include a description of practicable methods for determining the quantity, if any, of such drug in or on food, and any substance formed in or on food because of its use, and the proposed tolerance or withdrawal period or other use restrictions for such drug if any tolerance or withdrawal period or other use restrictions are required in order to assure that the proposed use of such drug will be safe. When data or other adequate information establish that it is not reasonable to expect the new animal drug to become a component of food, assay methodology is not required.

i. The kind of information required by this subdivision may include: Complete experimental protocols for determining drug residue levels in the edible products, and the length of time required for residues to be eliminated from such products following the drug's use; residue studies conducted under appropriate (consistent with the proposed usage) conditions of dosage, time, and route of administration to show levels, if any, of the drug and/or its metabolites in test animals during and upon cessation of treatment and at intervals thereafter in order to establish a disappearance curve; if the drug is to be used in combination with other drugs, possible effects of interaction demonstrated by the appropriate disappearance curve or depletion patterns after drug withdrawal under appropriate (consistent with proposed usage) conditions of dosage time, and route of administration; if the drug is given in the feed or water, appropriate consumption records of the medicated feed or water and appropriate performance data in the treated animal; if the drug is to be used in more than one species, drug residue studies or appropriate metabolic studies conducted for each species that is food producing. To provide these data, a sufficient number of birds or animals should be used at each sample interval. Appropriate use of labeled compounds (e.g. radioactive tracers) may be utilized to establish metabolism and depletion curves. Drug residue levels ordinarily should be determined in muscle, liver, kidney, and fat and where applicable, in skin, milk, and eggs (yolk and egg white).

As a part of the metabolic studies, levels of the drug or metabolite should be determined in blood where feasible. Samples may be combined where necessary. Where residues are suspected or known to be present in litter from treated animals, it may be necessary to include data with respect to such residues becoming components of other agricultural commodities because of use of litter from treated animals.

ii. If such new animal drug is one which has been shown to induce cancer when ingested by man or animal or after other tests which are appropriate for the evaluation of the safety of such drug and the Secretary is requested to find that, under the conditions of use specified in the proposed labeling and reasonably certain to be followed in practice, such drug will not adversely affect the animals for which it is intended and that no residue of such drug will be found in any edible portion of such animals, after slaughter or in any food yielded by or derived from the animal, methods of analysis shall be submitted in such form as to be suitable for publication in the Federal Register.

8. **Evidence to establish safety and effectiveness.**

   i. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the new animal drug is safe and effective for use as suggested in the proposed labeling.

   ii. An application may be refused unless it includes substantial evidence, consisting of adequate and well-controlled investigations including field investigation, by experts qualified by scientific training and experience to evaluate the effectiveness of the new animal drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the new animal drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

   iii. An application may be refused unless it contains detailed reports of the investigations, including studies made on laboratory animals, in which the purpose, methods and results obtained are clearly set forth of acute, subacute, and chronic toxicity, and unless it contains appropriate clinical laboratory results related to safety and efficacy. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the raw data are available in the application.

   iv. All information pertinent to an evaluation of the safety and effectiveness of the new animal drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, both favorable and unfavorable, involving the new animal drug that is the subject of the application, and related new animal drugs shall be submitted. An adequate summary may be acceptable in lieu of a reprint of a published report that only supports other data submitted. Include any evaluation of the safety or effectiveness of the new animal drug that has been made by the applicants veterinary or medical department, expert committee, or consultants.

   v. If the new animal drug is a combination of previously investigated or marketed new animal drugs, an adequate summary of preexisting information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components, shall be submitted. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted to the Food and Drug Administration by the applicant; with written authorization, information may also be incorporated from the material that another applicant has on file with the Food and Drug Administration. Each ingredient designated as active in any new animal drug combination must make a contribution to the effect in the manner claimed or suggested in the labeling, and, if in the absence of express labeling claims of advantages for the combination such a product purports to be better than either component alone, it must be established that the new animal drug has that purported effectiveness.

   vi. An application shall include a complete list of the names and post office addresses of all investigators who received the new animal drug. This may be incorporated in whole or in part by reference to information submitted under the provisions of 21 CFR 511.1.

   vii. Explain any omission of reports from any investigator to whom the investigational new animal drug has been made available. The unexplained omission of any reports of investigations made with the new animal drug by the applicant or submitted to him by an investigator or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources that would bias an evaluation of the safety of the new animal drug or its effectiveness in use, constitutes grounds for the refusal or withdrawal of the approval of an application.

9. **New animal drugs subject to section 512(n) of the act.** If the application is for a new animal drug subject to the certification provisions of section 512(n) of the act and the drug is included in regulations promulgated under section 507 of the act, the applicant may be exempted from the submission of some of the information required by subparagraph (8) of this paragraph if the application includes data adequate to prove that the new animal drug is comparable to the new animal drug for which certification has been previously provided.

10. Environmental Impact Analysis Report. The applicant is required to submit an environment impact analysis report analyzing the environmental impact of the ultimate use or consumption of the new animal drug pursuant to 21 CFR 25.1.

11. **Confidentiality of Data And Information In A New Animal Drug Application.** The availability for public disclosure of any record in the NADA file shall be handled in accordance with the provisions of 21 CFR 514.11.

    i. After approval has been published in the Federal Register certain data and information (as indicated in 21 CFR 514.11(e)) in the NADA file are immediately available for public disclosure unless extraordinary circumstances are shown. This information shall be known as a Freedom Of Information (FOI) Summary.

    ii. Preparation of the FOI Summary shall be by the applicant according to guidelines specified by the agency.

ATTACHMENT 2

INTERNAL BUREAU OF FOODS PROCESSING OF ANIMAL DRUG PETITIONS

INTERNAL BUREAU OF FOODS PROCESSING OF ANIMAL DRUG PETITIONS

(INADS, NADAs, and Master Files)

Petition Flow Process

1. The petition flow within the Bureau of Foods is depicted in Exhibit A.

2. A special messenger daily delivers new submissions and returns reviews between the Bureau of Veterinary Medicine (BVM) (Dr. Kingma's office) and the Bureau of Foods (BF) (Ms. Perez's office).

3. A new record-keeping and tracking system has been partially implemented by the Bureaus and should be fully operational in fiscal year 1977. The new system is expected to substantially reduce the clerical staff time now spent in recording information, improve the quality of the information recorded, and allow for more frequent reporting of status to the appropriate managers.

In the new system, preprinted record materials are attached to each petition in BVM, and the information is filled in by the BVM reviewer before submission to BF. The preprinted material includes two master cards and a tear-sheet with multiple stubs (See Exhibit B).[1] One of the master cards is permanently attached to the petition, and information is entered by various reviewers en route. The second master card becomes the BF master log maintained in the Office of the Associate Director for Sciences (SCI). The tear sheet stubs are used by each work station in BF to record a petition movement within the Bureau. For each movement, a stub with the petition number is initialed, dated, and the mail symbol of the unit to which the petition has been delivered is recorded. The stub is sent to SCI for attachment to a master card showing the current location of that petition.

The central log records not only the movement but also the number of days lapsed in each work station and the cumulative number of days in BF. Each month a listing is sent to each manager giving the petitions outstanding in his work unit, the number of days in his unit, and the total number of days the petition has been in BF.

4. Although the central processing records for BF are maintained in SCI, the master subject files are maintained in the Division of Toxicology by specially trained staff. These include a BF correspondence file for each petition and a cross-indexing system of drugs, sponsors and identification numbers. All petition jackets are returned to BVM after review. Therefore, the subject files are often relied upon for information in subsequent reviews to avoid recalling jackets unless necessary. Bureau staff are currently considering needs for scientific data storage and retrieval in BF and the possibilities of acquiring a

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[1] Not included.

computer terminal for the BF reviewers for direct access to the BVM computer information file.

5. All petitions are carried between work stations, avoiding the regular mail delivery, to assure no delays and to maintain security. In addition, all offices of the staff involved with petition review are locked at night to maintain security.

6. The initial routing of a petition submission is determined at the time of logging in SCI based on the information supplied with the petition by the BVM reviewer.

The Scientific Review Process

Before BF recommends approval of a new animal drug to BVM, concurrence is always required from the Division of Chemistry and Physics (DCH), the Division of Toxicology (DT), and the Associate Director for Sciences (SCI).

1. DCH has responsibility for evaluation of the following:

    A. Adequacy of the residue information and determination of the withdrawal period.

    B. Adequacy of the proposed regulatory method of analysis for residues.

    C. Adequacy of information on the metabolism of the drug (in conjunction with DT).

When the proposed regulatory method and residue data involve a microbiological assay, e.g. for an antibiotic, BVM has responsibility for the adequacy of these data. However, DCH in conjunction with DT considers the question of drug metabolism and the assignment of conditions for the assay which include the target tissue, compounds to be measured, and the required lower limit of measurement.

The DCH team leader for animal drug review assigns a primary reviewer for each petition. On completion of the review, a response is prepared to the Assistant Director for Petition Review in DT. A rough draft of the response is reviewed with the DCH team leader and the Chief of the Residue Analysis and Method Investigation Branch (RAMIB) before final typing. Frequently, the reviewers in the unit will exchange and critique each other's reviews to take advantage of the various expertises within the review unit. Another advantage of this practice is to provide general familiarity with the petition by more than one reviewer, so that in the absence of the primary reviewer, another staff member is available to handle questions.

Occasionally, a rough draft is discussed with a reviewer in DT, when questions of mutual interest need to be clarified before a conclusion is reached. This most frequently occurs in recommendations for granting a withdrawal period for INAD use or in the review of metabolism data where decisions involve both toxicology and chemistry judgments.

Following the supervisory approval of the team leader and Chief of the RAMIB, the response is returned to the primary reviewer, typed in final form, signed by the reviewer, and transmitted to DT.

2. DT is responsible for the following:

    A. Adequacy of the toxicology data.

B. Assignment of the "safe" level of residue or tolerance, or alternatively, assignment of the lower limit of measurement required for the regulatory method of analysis for residues to assure food safety.

C. Overall responsibility to determine when all requirements on food safety have been satisfied.

DT shares responsibility with DCH to determine the adequacy of the metabolism data.

When DT determines the "safe" level of residue, DCH recommends a withdrawal period based on the residue data. In the case of an INAD where the human safety data are incomplete for NADA approval, judgments on withdrawal for investigational use are made jointly considering the limitations in both the chemistry and toxicology information.

DT has responsibility for preparing the BF response to BVM. Accordingly, the response is from the DT reviewer, through the DT Assistant Director for Petition Review and the Associate Director for Sciences to the BVM reviewer.

The rough draft of the response is reviewed by the DT team leader before final typing. When the response to BVM is completed in DT and signed by the reviewer and supervisors, it is transmitted to SCI.

3. The BF program manager for animal drugs provides a policy review for the Bureau and has delegated authority to sign off all responses for SCI. Any petition which involves the setting of a new precedent or major deviation from usual policy will be referred to the Associate Director for Sciences for his approval. Following approval in SCI, the response is transmitted to BVM.

4. Any reviewer has the option of requesting consultation or special review of particular data by a subject matter expert in the Bureau. For example, in DCH this may be a mass spectrometry expert, a polymer chemist, a heavy metals analytical specialist, a pesticide chemist, etc. In DT, it may be a specialist in teratology, mutagenesis, neuropharmacology, etc., or a request may be made of the Division of Pathology for a special review.

Statistical analysis is always conducted on the data from a method validation trial. The DCH and DT reviewers may request special statistical review by the Division of Mathematics on any data where they feel it is advisable before a conclusion is reached.

Some petitions raise questions about an area of microbiology or questions of the nutritional integrity of food from drug-treated animals. Therefore, a review or consultation with appropriate staff in the Division of Microbiology or the Divisions of Nutrition and Consumer Services may be sought.

Each assigned reviewer in DCH and DT has the responsibility to alert his supervisors and the BF program manager when a petition raises policy issues or administrative and legal questions that need to be resolved prior to completing the BF recommendation. Arrangements can then be made to resolve these issues while the scientific review proceeds concurrently.

5. In any complex scientific area, there will on occasion be differences of scientific opinion among the staff. The procedures in BF for resolving such differences utilize the line organization authority. For example,

when a reviewer in DCH and a reviewer in DT have a difference of opinion which is not resolved in joint conference with the respective team leaders, the issue is reviewed first by the next line supervisors and ultimately is reviewed by the respective Division Directors, if necessary. The Associate Director for Sciences may or may not initially participate in a Division Director's review.

Generally, Division Directors are not involved in a given petition review unless controversy arises. Therefore, it is requested that when a drug sponsor opposes the conclusions reached by the Bureau on a human safety question and plans to appeal the decision to the Director of the Bureau of Foods, that the matter first be brought to the attention of the BF program manager so that arrangements can be made for a briefing on the issue to the Division Directors and the Associate Director for Sciences for their consideration.

Informal exchange of ideas and information is encouraged between the reviewers in BF and BVM. When a major disagreement occurs between the two Bureaus which can not be resolved by the reviewers, the BF program manager arranges for a BF re-evaluation of the issue by the line managers. If a major policy issue is involved, the matter may be placed on the agenda for the regularly held joint BVM-BF Director and staff meetings or presented to the Working Group on Animal Drugs, chaired by the Deputy Commissioner.

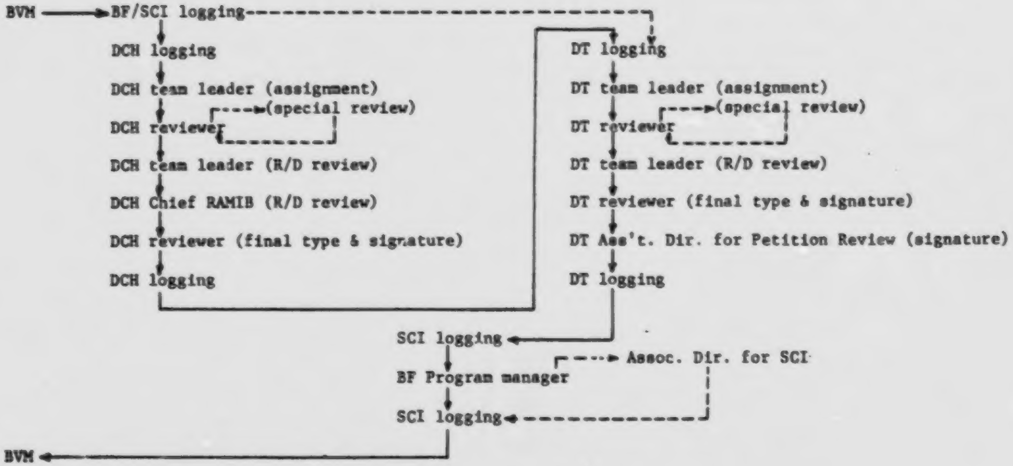
Petition Assignments and Priority

The assignment of primary reviewers for each petition in DCH and DT by the team leaders is based primarily on current workload for each reviewer and past experience or expertise with the particular type of drug. Whenever possible, continuity on sequential submissions is maintained with the original reviewer, although workload consideration and training of reviewers may affect the assignment decisions.

Petitions are handled on a priority basis by date of receipt by the reviewer, unless there is a valid reason mutually agreed upon by BVM and BF management. Because each reviewer at any time will have a number of petitions assigned, he may elect while conducting an extensive review of one petition or awaiting additional information, to handle a relatively short submission out of sequence. For this reason, reviews of protocols or INADs may be completed while an extensive review of a new NADA with prior data of receipt, is in progress. The review of data submitted to Master Files or in Drug Experience Reports are generally given lower priority than INAD and NADA submissions, unless the data are critical to a pending NADA and INAD approval.

In addition to the above guidelines, the Bureau managers utilize the monthly status reports on outstanding petitions to focus on priority.

Petition Flow Process in the Bureau of Foods, Exhibit A.


BVM
BF/SCI logging
DCH logging
DCH team leader (assignment)
DCH reviewer
(special review)
DCH team leader (R/D review)
DCH Chief RAMIB (R/D review)
DCH reviewer (final type & signature)
DCH logging
DT logging
DT team leader (assignment)
DT reviewer
(special review)
DT team leader (R/D review)
DT reviewer (final type & signature)
DT Ass't. Dir. for Petition Review (signature)
DT logging
SCI logging
BF Program manager
Assoc. Dir. for SCI
SCI logging
BVM

Bureau of Veterinary Medicine (BVM)
Bureau of Foods (BF)
Office of the Associate Director for Sciences (SCI)
Division of Chemistry and Physics (DCH)
Division of Toxicology (DT)
Residue Analysis and Methods Investigation Branch (RAMIB)
Rough Draft (R/D)
——— represents usual route
- - - - - represents alternative route

ATTACHMENT 3

REGULATION OF ESSENTIAL NUTRIENT ADDITIONS TO ANIMAL DIETS

D. E. Ullrey[1]

The Federal Food, Drug, and Cosmetic Act as amended (FDA, 1979a) does not include a definition of essential nutrients for animals. The term "animal feed" has been interpreted to include this class of substances, and essential nutrient additions to animal diets have been regulated as food additives or through qualification for the GRAS (generally recognized as safe) list. This position requires that individuals who wish to fortify animal diets with nutrients recently recognized (since 1958) as essential must file a petition with the Food and Drug Administration (FDA), proposing issuance of a regulation prescribing the conditions under which such additives may be safely used. Since nutrients are not usually proprietary substances, individual companies are loathe to make the financial investments necessary to gain FDA approval for their use. This problem has caused particular difficulties as animal production systems have changed, leading to deficiencies of certain nutrients-such as selenium - which previously were of little concern.

Selenium – A Model Case

Selenium is a semimetal which is very similar to sulfur in its chemical properties. It exists in soil as basic ferric selenite, calcium selenate, elemental selenium, and organic compounds derived from plant and microbial tissue. Its availability for uptake by plants is greater in alkaline soils than in acid soils, and certain plants accumulate the element in quantities which are toxic to animals which eat them. Much of the early interest in selenium among nutritionists concerned this very issue. Marco Polo referred in his journals to "...a poisonous plant...which if eaten by (horses) has the effect of causing the hoofs...to drop off" (Polo, 1926). In 1857, Dr. T. C. Madison, a U.S. Army surgeon at Fort Randall, Nebraska Territory, described similar signs in horses which he attributed to "alkali disease" (Madison, 1860). Selenium was identified as the toxic principle by scientists from the U.S. Department of Agriculture and the South Dakota and Wyoming State Agricultural Experiment Stations through a series of studies begun in 1929 (Franke, 1934). Not until 1957 (Schwarz and Foltz, 1957; Patterson et al., 1957; Scott et al., 1957; Stokstad et al., 1957) was the role of selenium as an essential nutrient established. Kubota et al. (1967) subsequently determined that the selenium-deficient areas of the United States are much larger than those areas which are selenium-toxic.

Deficient diets result in a number of signs that can be prevented by supplemental selenium. These include liver necrosis (Schwarz and Foltz, 1957; Eggert et al., 1957), exudative diathesis (Patterson et al., 1957), and myopathy (white muscle disease) (Muth et al., 1958; Hogue, 1958; Hartley and Grant, 1961). Species in which deficiency signs have been demonstrated include mice, rats, guinea pigs, rabbits, chickens, turkeys, quail, swine, sheep, cattle, horses, dogs, deer, and squirrel monkeys. Growth responses to selenium supplements have been reported in children with kwashiorkor (Schwarz, 1967; Majaj and Hopkins, 1966). In 1973, workers at the University of Wisconsin established that selenium is an integral part of the enzyme glutathione peroxidase, which functions importantly in protecting cell membranes against peroxidative damage (Rotruck et al., 1973). This enzyme is present in the tissues of all higher animals, including humans.

Selenium Deficiency On Farms

Dramatic changes have been made in the management of food animals over the past 20 years. Most poultry, swine, dairy cattle, and finishing beef cattle are now raised with limited use of pasture. This change, plus less use of other green forages, has decreased intakes of vitamin E. Since the need for selenium is related to the dietary supply of vitamin E, animals raised under intensive management in selenium-deficient areas frequently exhibit deficiency signs when not supplemented with selenium and vitamin E (National Research Council, 1971).

Michigan State University scientists first diagnosed the deficiency in commercial swine herds in Michigan in 1967 (Michel et al., 1969). Since other diseases bear some resemblance to this deficiency, it is likely that the deficiency was present, but undiagnosed, much earlier (Trapp et al., 1970). Sudden-death losses were common in pigs shortly after weaning, and controlled studies suggested that mortality ranged from 15 to 20 percent, while deficiency lesions were present in 25 percent or more. Impaired reproductive efficiency was also evident (Ullrey, 1974).

Similar practical problems were reported in commercial turkey flocks in southwestern Ohio in 1964 (Scott et al., 1965). Poor growth, increased mortality, and gizzard myopathy were seen in young poults. In the presence of vitamin E, a selenium requirement of 0.18 ppm was established. In 1967, Thompson and Scott showed that even when generous amounts of vitamin E were present, selenium was still essential for the chick and quail, and a year later (Thompson and Scott, 1968) these Cornell scientists recommended that poultry feeds which were not supplemented with a stable form of vitamin E should contain selenium at a concentration of at least 0.15 ppm, a figure which was 0.1 ppm greater than most commercial poultry feeds in that region.

Petition For GRAS Status For Selenium

The increasing incidence of selenium deficiency in the nation's herds and flocks during the 1960s stimulated the American Feed Manufacturers Association (AFMA) to petition FDA for GRAS status for selenium, so that supplements might be legally added to animal diets. The petition was prepared by the AFMA Director of Feed Control and Nutrition and was submitted March 9, 1970. Supplements to the petition were provided on March 31, April 21, May 11, May 18, May 21, and October 1, 1970. On September 23, 1970, the Director of the FDA Bureau of Veterinary Medicine (BVM) acknowledged receipt of the petition and several of the supplemental submissions. The BVM Director concluded that GRAS status had not been established and proposed in this and a subsequent letter (dated November 24, 1970) that studies should be conducted with target species to establish whether selenium supplements would increase selenium concentrations in edible tissues of animals which were not initially deficient. This proposal was based on the 1962 Drug Amendments (Public Law 87-781) of the Federal Food, Drug, and Cosmetic Act (FDA, 1979a) which required that chemicals used in feed for food-producing animals must not adversely affect the animals nor result in a residue in products used for human food if the chemicals posed a carcinogenic risk.[2]

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[1] Professor, Dept. of Animal Science, Michigan State University, East Lansing.

The AFMA Director of Feed Control and Nutrition replied to the BVM Director on December 21, 1970, by submitting published data on (1) ranges of selenium levels in typical turkey, chicken, and swine feeds, (2) normal background levels of selenium in tissues of poultry and swine, (3) the effect of recommended selenium supplements in poultry and swine diets on human selenium intakes, and (4) tissue selenium levels in poultry and swine fed practical diets supplemented with selenium. Since comparable data were not available for ruminants, the original petition was amended to include only poultry and swine. However, the petitioners reaffirmed their belief that this submission satisfied the existing and proposed GRAS criteria (FDA, 1970). The official notice of filing of the petition was published in the Federal Register Thursday, June 17, 1971 (FDA, 1971), although the GRAS issue was replaced by a proposal to establish a food additive regulation governing "...the safe use, as a nutrient, of selenium from sodium selenite or sodium selenate in the feed of chickens, turkeys, and swine...."

Food Additive Regulation For Selenium For Swine And Poultry

During the period that the AFMA petition was being developed and for some years afterward, a number of researchers were conducting controlled studies to develop data for submission to FDA. Since selenium was not an approved food additive, these studies were conducted under "investigation of new animal drug" (INAD) numbers issued by FDA. Regulatory activity was also coordinated with the Meat and Poultry Inspection Service of USDA. Experimental animals fed supplemental selenium could not be used for human food, and their carcasses or products were denatured and destroyed. After sufficient data were acquired to satisfy FDA and USDA of the safety of the practice, human food use was permitted after a 60-day selenium withdrawal.

On April 19, 1973, a Draft Environmental Impact Statement (FDA, 1973a) was published by FDA in compliance with the requirements of the National Environmental Policy Act. A proposed food additive regulation was published 8 days later (FDA, 1973b). By the end of the comment period (June 26, 1973), the FDA Hearing Clerk had received 19 comments on the environmental impact statement and 143 comments on the regulation. Of the 143 comments, 65 were from private citizens, 40 from feed and associated industries, 12 from trade associations, and 26 from university scientists. Responses were judged 73 in favor, 68 opposed and 2 noncommital. Of the 40 feed and related industry comments, 38 favored selenium supplements, one was opposed, and one was noncommital. All 12 trade association comments favored the proposal, as did 22 of the 26 university comments; 3 were opposed, and one was noncommital. One of the 65 comments from private citizens was in favor, while the remainder were opposed.

After the submission of further data, and deliberation by FDA, the availability of the Final Environmental Impact Statement--Selenium in Animal Feeds was announced in the Federal Register on Tuesday, January 8, 1974 (FDA, 1974b). The final food additive regulation was also published that day (FDA, 1974a). It took effect on February 7, 1974, 17 years after the discovery of the essential nature of selenium, and 4 years after submission of the original petition to FDA. (Parenthetically, New Zealand's Governor-General authorized selenium supplementation under medical or veterinary prescription in 1959 (Governor-General, 1959)).

Food Additive Regulation For Selenium For Ruminants

Despite the discovery in 1958 (Muth et al., 1958; Hogue, 1958) that selenium would protect against white muscle disease in young ruminants, and the generally recognized benefit of injectable vitamin E-selenium preparations for young lambs and calves, it was still not legal to supplement deficient ruminant diets in 1975. On August 29, 1975, the Assistant Director of the Ohio Agricultural Research and Development Center, Wooster, wrote to a number of agricultural experiment station directors and animal science department chairmen, enlisting their support in establishing a Selenium for Ruminant Animals Task Force. Initial members of the Task Force included scientists from Purdue University, Virginia Polytechnic Institute and State University, University of Illinois, Ohio Agricultural Research and Development Center, Oregon State University, and Michigan State University. Their efforts were coordinated by the Assistant Director of the Ohio Agricultural Research and Development Center in consultation with the AFMA Director of Feed Control and Nutrition and a representative of FDA-BVM.

The Task Force held its first meeting at the O'Hare Hilton in Chicago on October 23 and 24, 1975. The previously designated scientists were present, plus representatives from the University of Florida and the University of Missouri. A representative from the University of Wisconsin joined the Task Force later. This group assumed responsibility for assembling published information and developing new data in the preparation of a supplemental food additive petition to permit the addition of selenium as sodium selenite or selenate to the diets of sheep and cattle at a level of 0.1 ppm. Some research was already underway. Additional research was initiated, and preparation of the petition began immediately.

The Task Force found that evidence of selenium-responsive disease in the field was overwhelming; according to one survey (Wolf et al., 1963), white muscle disease had been diagnosed in lambs and calves in 30 of the 50 United States. Agricultural statistics showed that approximately 51 percent of the beef cattle, 69 percent of the dairy cattle, and 31 percent of the sheep produced in 1975 in the United States were produced in selenium-deficient states. Economic losses to livestock producers were associated with death losses, impaired reproductive efficiency, and, in some cases, reduced growth, feed efficiency, and production of milk and wool. Total losses during 1975 to producers of beef cattle, dairy cattle, and sheep were estimated to be nearly $545 million (Selenium for Ruminants Task Force, 1976).

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[2] Six published studies (National Research Council, 1976) have examined the issue of selenium as a carcinogen. Three studies alleged that this element was carcinogenic, while three drew the opposite conclusion. A critical evaluation of these six trials revealed significant errors in experimental design, unusually high levels of selenium and/or infectious disease in the three studies in which carcinogenicity was indicated. The remaining three studies, which were well controlled investigations, found no evidence of carcinogenic activity. Scientists in FDA and the National Cancer Institute concluded that "judicious administration of selenium derivatives to domestic animals would not constitute a carcinogenic risk" (FDA, 1973b).

On March 31, 1977, the first edition of the supplemental petition was submitted to FDA. Subsequent editions ultimately included the following sections:

(1) Indications of selenium-responsive disease in the field, including reports from veterinary diagnostic laboratories.
(2) Justification for adding selenium to the diets of ruminants.
(3) Selenium content of grains and forages in relation to the selenium requirements of ruminants.
(4) Safety of selenium when fed at a level of 0.1 ppm to cattle and sheep.
(5) Analytical methods for selenium.
(6) Proposed methods of feeding selenium to sheep, dairy cattle, and beef cattle.
(7) Research data from Task Force members.
(8) Estimate of effects on human health from consumption of tissue from ruminants consuming feed containing selenium at 0.1 ppm
(9) Environmental and economic impact analysis.

On Tuesday, March 21, 1978 (FDA, 1978a), an amendment to the selenium regulation was published, permitting supplementation of the diet of ewes and ewes with lambs up to 8 weeks of age. Notice was given in the Federal Register on April 7, 1978 (FDA, 1978b), that a food additive petition had been filed by AFMA (for the Task Force) proposing that the use of supplemental selenium be extended to diets of sheep and of beef and dairy cattle. A further amendment was published on Friday, January 26, 1979 (FDA, 1979b), including beef, dairy cattle, and all ages and sexes of sheep. The final regulation thus included the following features:

Selenium (as sodium selenite or selenate) may be added to feed as follows:

(1) Poultry
    (a) In complete feed of growing chickens up to 16 weeks of age at a level not to exceed 0.1 ppm.
    (b) In complete feed of turkeys at a level not to exceed 0.2 ppm.
(2) Swine
    (a) In complete feed at a level not to exceed 0.1 ppm.
(3) Sheep
    (a) In complete feed at a level not to exceed 0.1 ppm.
    (b) In a feed supplement for limit feeding at a level not to exceed an intake of 0.23 mg/head/day.
    (c) Up to 30 ppm in a salt-mineral mixture for free-choice feeding at a rate not to exceed an intake of 0.23 mg/head/day.
(4) Beef cattle
    (a) In complete feed at a level not to exceed 0.1 ppm.
    (b) In a feed supplement for limit feeding at a level not to exceed an intake of 1 mg/head/day.
    (c) Up to 20 ppm in a salt-mineral mixture for free-choice feeding at a rate not to exceed an intake of 1 mg/head/day.
(5) Dairy cattle
    (a) In complete feed at a level not to exceed 0.1 ppm.

Epilogue

It has taken 22 years from the discovery of the essential nature of selenium to gain approval from FDA to add this nutrient to the diets of certain poultry, swine, sheep, and cattle. This period includes 12 years during which the efforts of large numbers of scientists were directed specifically toward this goal. The research cost cannot be precisely estimated, but the specific projects involving the Selenium for Ruminants Task Force were budgeted at $173,124[3] for a 1-year period in 1976 and 1977 (Johnston, 1976). It would certainly be conservative to suggest that the effort expended so far in meeting regulatory requirements for selenium has cost over a million dollars. The inability to supplement demonstrably deficient diets during this period has cost hundreds of millions. Further effort is still needed and is continuing, since addition of selenium to diets for laying hens producing eggs for human consumption has not yet been approved by FDA.

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[3] This amount includes some costs of graduate assistants and technical assistance but not the salaries of senior scientists.

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IMPACT OF GOVERNMENT REGULATION ON THE DEVELOPMENT OF CHEMICAL PESTICIDES FOR AGRICULTURE AND FORESTRY

Council for
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FOREWORD

As the Nation enters a period of increasing financial stress, due in part to government actions, including those taken by regulatory agencies, members of the public are becoming increasingly aware that the cost-benefit concept has application to government regulations. Regulations have benefits, but they also have costs. Through education regarding such matters, society will be enabled to adopt a position in which the benefits are well in excess of the costs.

Because of a desire to increase the general level of understanding regarding the impacts of government regulations on the development of agricultural chemicals, the executive committee of the Council for Agricultural Science and Technology (CAST) authorized the distribution of a mail ballot to members of the board of directors in November 1978 to determine whether a task force should be established to prepare a report dealing with the impacts. The board approved, and the task force was promptly established. The task force included expertise in agricultural economics, agronomy, animal science, dairy science, entomology, meat science, nematology, plant pathology, poultry science, range management, sociology, soil science, toxicology, and weed science.

This report, the second of two prepared by the task force, deals primarily with regulation of chemical pesticides for agriculture and forestry. The first, dealing with animal drugs and nutritional supplements and to a minor extent with pesticides used in animal production, was issued as Report No. 85 in October 1980.

The first draft of this report was reviewed by a subcommittee of the task force at a special meeting, and a revised version was sent to the headquarters office for editing. Editing was done by Dr. L. L. Danielson with assistance from the headquarters office, and the edited version was returned to the task force and the CAST executive committee for review and comment. Two more revised versions were then returned to the task force, and one was sent to the CAST editorial review committee for further comments before the final version was reproduced for publication.

On behalf of CAST, I thank members of the task force, the editorial review committee, and all the others who gave of their time and talents to prepare this report as a contribution of the scientific community to public understanding. Thanks are due also to the employers of task force members who made the time of their employees available at no cost to CAST. And finally, thanks are due to members of CAST. The unrestricted contributions they have made in support of the work of CAST have financed the report.

This report is being distributed to members of Congress, officials in the U.S. Department of Agriculture and the Environmental Protection Agency, the media, and institutional members of CAST. Individual members may receive a copy on request.

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Charles A. Black
Executive Vice President
Council for Agricultural
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PREFACE

This is a report of the Task Force on the Impact of Government Regulation on the Development of Agricultural Chemicals. The Task Force has organized and focused its efforts in two areas: (a) chemicals used in animal production and (b) chemical pesticides for agriculture and forestry. The Task Force decided fairly early in its deliberations not to consider fertilizers.

This report has been prepared by the Task Force Subcommittee on Chemical Pesticides for Agriculture and Forestry. It has been read and approved by the membership of the entire Task Force.

The Task Force held meetings on January 29 and 30, 1979, in Washington, D.C., and on April 17 and 18, 1979, in Atlanta. The two subcommittees each held additional meetings to discuss and revise their findings. The Task Force held discussions with staff members of the Food and Drug Administration (Bureau of Foods and Bureau of Veterinary Medicine), the Environmental Protection Agency, the USDA Food Safety and Quality Service, the National Agricultural Chemicals Association, the American Feed Manufacturers Association, the Animal Health Institute, the Fertilizer Institute, and the Environmental Defense Fund. Consultations were held with individual government, industry, and university scientists by individual Task Force members. The Task Force has appreciated the interest and cooperation of the representatives of government, industry, public-interest groups, and individual scientists who have made the report of the Task Force possible. Any errors or misinterpretations of the information incorporated in this report are, however, the Task Force's own responsibility.

The Subcommittee on Chemical Pesticides for Agriculture and Forestry included Eldon I. Zehr (Chairman), Samuel R. Aldrich, Thomas Allen, Arnold P. Appleby, Gerald A. Carlson, Don A. Dillman, David A. Graham, Ronald J. Kuhr, John D. Radewald, and Robert J. Weir. The Subcommittee on Chemicals for Animal Production included Charles A. Lassiter (Chairman), Gerald A. Carlson, Edward C. Naber, Albert M. Pearson, Duane E. Ullrey, and Robert J. Weir.

Vernon W. Ruttan
Task Force Chairman

SUMMARY

Cultural practices and biological techniques, including development of new plant varieties, are useful in controlling many pests and diseases of plants. These alternatives, however, are not always available, effective, or practical. Chemical pesticides are needed to maintain consistent control of plant pests and diseases when other methods are not appropriate. In recent years, the use of chemical pesticides has been subject to increasingly stringent regulations designed to protect the health of consumers and producers and to limit undesirable environmental impacts. This report examines the impacts of government regulation on the development of chemical pesticides for agricultural and forest uses.

Government regulation has created lengthy delays in registering and reregistering chemical pesticides. Moreover, it has caused sharply higher costs of developing new chemical pesticides and of defending chemical pesticides now marketed. These increased costs are passed on to users, including farmers, foresters, home gardeners, and industrial firms, and in the end lead to higher costs of food, fiber, ornamentals, and lumber to consumers.

The chemical industry has responded to increased stringency of regulation by hiring more employees and completing the additional testing required for registration. There is little evidence that government regulation is causing firms to abandon pesticide research and development in favor of more lucrative investments; in fact, pesticide chemical research and development expanded in real terms each year from 1967 through 1978. Chemical pesticides continues to be a growth industry. However, the percentage of funds allocated for synthesis, screening, and field development of new materials has decreased, while more funds have been spent meeting registration requirements.

The number of new compounds registered annually for commercial uses declined after responsibility for registration was transferred to the Environmental Protection Agency in 1970, and several years after the Federal Environmental Pesticide Control Act was enacted in 1972. Administrative difficulties encountered in registering new compounds are a continuing source of frustration for manufacturers and distributors of chemical pesticides as well as for researchers. Recent developments suggest that some of the problems associated with pesticide regulation are being resolved.

Shifts in emphasis of research and development in pesticides are a source of concern. As costs have risen, manufacturers have shifted their efforts toward major crops and major uses, with the result that chemicals having a broad spectrum of pesticide activity have been emphasized at the expense of chemicals that are more specific in their activity. This shift could be harmful to beneficial organisms and may affect the progress and development of integrated pest management, in which chemicals of specific activity are needed to avoid harm to beneficial organisms that contribute to control of the pests.

The outlook for biological control of plant pests improved substantially after certain important biological control agents were exempted from most pesticide registration requirements. Current regulations favor the development of biological control agents, except for certain chemicals of biological origin which remain subject to pesticide registration requirements. Since many of these, such as sex attractants, are of a highly specific nature, registration costs may be prohibitive. However, more lenient registration requirements now being developed may alleviate many of the problems in biological control.

Provisions of the Federal Pesticide Act of 1978 seem adequate to address the needs of pest management and biological control. Enlightened cooperation among federal regulatory agencies, university research and extension agencies, state and local governments, and manufacturers, distributors, and users of chemical pesticides could overcome the problems of minor uses and the need for pesticides with a limited toxicological spectrum.

Actions of regulatory agencies have not always contributed to their objective of reduced pesticide use. Sometimes chemicals removed from the market as a result of regulatory action have been replaced with chemicals that must be used in greater volume or more frequently or with greater hazard to achieve equivalent pest control. In some instances, government agencies appear not to have considered all the factual evidence before regulatory decisions were made. These incidents are unfortunate because they are not in the public interest, and they undermine confidence in the credibility of both the regulatory agencies and the pesticide industry to deal with problems of pesticide use in fairness to all parties concerned.

An important indirect cost of chemical pesticide regulation is the diversion of university and USDA scientists from innovative research and extension education. Personnel and funds diverted from agricultural research and extension are important long-range costs because returns to society from agricultural research and extension traditionally have been among the best of long-term public investments.

INTRODUCTION

Prior to the mid-1920s, technical progress in American agriculture was directed primarily to the achievement of increases in output per worker through advances in mechanical technology. During the last half century, advances in mechanical technology have been complemented by new biological and chemical technologies directed to improving the quality and increasing the output per unit of land area at reduced cost per unit of output.

Since the early 1960s, there has been heightened concern about the effect of the new technologies or innovations on the health and safety of agricultural producers and consumers and on the quality of the products and the environment. The result has been the emergence of a series of institutional changes represented by new laws and regulations designed to achieve more effective social control over the development and use of the innovations.

Both the drive for *technical innovation* leading to increased productivity of plants and animals and the drive for *institutional innovation* resulting in constraints on the development and use of the new technologies have been generated by powerful economic and social forces. Increasing scarcity of land and water resources, reflected in rising agricultural land values and rising costs of land improvement, is continuing to create a strong need for yield-increasing technologies in agriculture — for higher output per acre. The rising value that society is placing on health and environmental quality has led to a demand for more effective social controls over the development and use of new technologies.

This report attempts to assess the impact of the new regulatory regimes that have emerged over the last decade on innovation in chemical pesticides for agricultural and forest uses. This is only a small part of the broader issues referred to in the preceding paragraphs. The report is dedicated, however, to the proposition that it is in the interests of society to develop and use the potential opened up by advances in the application of new technologies to agricultural production as well as to manage this potential. Ideally, the societal payoff of advances in agricultural productivity, the health and safety of agricultural producers and consumers, and the quality of the environment will all be valued realistically as laws and regulations are developed.

Americans have been favored with an abundance and a wide variety of foods, and, as a consequence, the productivity of American agriculture is generally taken for granted. Part of the success of the American food production system stems from the natural fertility of many of the soils and from the ability of American farmers to produce large quantities of food with relatively little labor input. But even the most fertile soil must be protected from erosion and in time must be replenished with nutrients. Mechanized farming depends upon abundant and economical sources of energy. Farming efficiency has increased with size and specialization. But concentrated and continuous production of a single crop increases the potential for outbreaks of insects, weeds, disease organisms, and other pests. To support crop production and marketing activities, a strong agribusiness enterprise is necessary to provide equipment, seeds, fertilizers, pesticides, fuel, markets, and transportation. The results of agricultural research must be applied to sustain and increase the output of food, fiber, ornamentals, and lumber.

Production of crops and forest products is but one example of the interdependency among the several sectors of the American economy. Actions that affect one small segment often may have an impact on the whole of American society. Thus, chemical pesticides constitute only a small fraction of the total agricultural and forest products enterprise even though the annual business is valued in excess of $3 billion (National Agricultural Chemicals Association, 1978). However, disruption of the supply of these chemicals without suitable replacement would impact severely on the total supply of agricultural and forest products, and even more so on the stability of the outputs.

Stability of production is a quality that often is overlooked. The security and welfare of all nations is heavily dependent upon the assurance of a steady, reliable source of food. Threats of pests and diseases constitute one of the most destabilizing influences on crop production worldwide. Pest control practices, including pesticides, are very important for assurance of year-to-year stability of production (Carlson, 1979).

In the following discussion, the focus is primarily on the impact of government regulation on the development of chemical pesticides for agricultural and forest uses. Government regulation has important influences on commercial fertilizers as well, but the regulatory environment is so different that pesticides and fertilizers need to be considered separately.

Four major groups of chemicals other than fertilizers are used in production of crops and forest products: insecticides, herbicides, growth regulators, and chemicals for disease control which include fungicides, nematicides, and bactericides. Some of these chemicals are effective on more than one type of pest; e.g., some fungicides may also have nematicidal properties. In addition, predacides, rodenticides, piscicides, defoliants, and desiccants contribute significantly in some instances.

Insecticides are important for a steady supply of farm products year after year. They have helped to avoid frequent catastrophic losses of crops to plagues of insects. Together with similar methods for avoiding losses due to diseases, insecticides have enabled commercial production of fruits and vegetables on a much larger scale than was possible only a few decades ago. Sometimes insecticides have been used when they were not required, and some have been injurious to natural parasites and predators. Sometimes crop production has relied too heavily on the use of insecticides. Recent concepts of integrated pest management have the potential to reduce the scale and indiscriminant use of, but not the need for, insecticides.

Widespread use of herbicides is a more recent innovation than the use of insecticides. Herbicides, used to kill weeds, have become the most widely used pesticides in agriculture for several reasons. First, weed control with herbicides often is superior to that obtained by mechanical means alone, reducing competition of weeds for moisture and nutrients, and thus increasing crop yields. Second, fewer trips through fields are necessary, less labor is required, and savings in fuel and deterioration of equipment result. Third, herbicides do not physically disturb the soil, and they may be used in systems that leave residues of plant debris on the soil surface; thus they contribute to reduced water and wind erosion. And fourth, appropriate herbicides do not injure roots of crop plants as does cultivation; consequently, crop yields may increase.

Growth regulators have fewer general uses in agriculture, but are nonetheless important. Growth regulators may save much hand labor, as in removing excessive numbers of fruits on fruit trees. They are also used to adjust maturity dates of plants, and to help provide a uniform supply of produce for processing. Some are used as defoliants or desiccants to improve harvesting efficiency and quality of harvested products.

Chemical pesticides often are used to help control plant diseases and nematodes. Plants are especially vulnerable to diseases when grown together in large concentrations, as was evident in the potato famine in Ireland and other European countries in the 1840s, and more recently in the southern corn leaf blight epidemic in the United States. One basic feature of American agriculture is a high concentration of a single variety of plants in the limited geographic area to which it is best suited. Foods from these plants often must travel long distances to the consumer. Some require protectant chemicals as well as controlled environments to reduce spoilage in transit and during storage to assure adequate supplies throughout the year. An effective and diverse supply of chemical pesticides is needed to contain threatening plant diseases that might otherwise devastate American crops. Chemical pesticides are the principal means for effective control of certain plant diseases — notably those of fruits and vegetables — when plants are grown together in large concentrations.

One of the major reasons that new pesticide compounds are needed is that, in time, existing pesticides may lose their effectiveness. Resistance to most types of insecticides, to some kinds of miticides and fungicides, and possibly to certain nematicides has developed in some pest species in the past 20 years [see Brown (1971) and Ogawa et al. (1977) for a listing of resistant pest species, and Carlson (1977) for evidence on the effect of insect resistance on the demand for substitute insecticides]. There is also growing recognition of the effect of herbicides on selection of weed species which are more difficult to manage. Although such biological depletions can be limited by judicious use of current pesticides, new compounds must be developed continually to maintain effective means of pest control.

Numerous laws and regulations have been implemented to protect workers, consumers, and the environment from adverse effects of pesticides. These laws and regulations were necessary because many hazardous materials were being produced, distributed, and used without adequate investigation of their effects on human health and safety and on the environment. The primary purpose of the legislation was to correct such abuses. Now that safeguards have been implemented, perhaps it is time to evaluate their long-term effects.

Research and development are essential for improvement of chemical pesticides and their uses in agriculture and forestry. Agricultural research in the United States and worldwide has a high rate of return in increasing the output of food and fiber (Evenson et al., 1979; Nuckton, 1979). Chemical pesticides rendered ineffective through resistance mechanisms will need to be replaced. Through research, safer products can be developed. Chemical pesticides can be applied more efficiently and effectively, and they can be made more specific so that beneficial organisms are not harmed. Their persistence and threats to components of the environment can be reduced. More effective control of target pests can be obtained. Much of this research and development must be done by private industry cooperating with public and private research centers and with the federal and state governments. Does the present atmosphere encourage or hinder progress toward safer, more effective chemicals? What are the consequences of current government regulatory activities? What is the outlook for pesticides in the near future? We explore answers to these and other questions in the following pages.

Information on the impacts of government regulation on development of chemical pesticides for agriculture and forestry is sketchy and fragmented. Often it is based on conjecture, projection of short-term information to long-term trends, and on facts that can be interpreted several ways depending on the viewer's overall perspective. We attempted to overcome these problems by consulting with representatives of the chemical pesticide industry, the Environmental Protection Agency, the Environmental Defense Fund, and the Food and Drug Administration, and with respected colleagues in the scientific community. For published information we have relied heavily on reports published by the National Agricultural Chemicals Association and the Environmental Protection Agency. We also studied reports published by the National Academy of Sciences (1975), the National Research Council (1975, 1978), and a study report on the use of chemicals to control plant diseases prepared by the American Phytopathological Society (1979) for the Environmental Protection Agency, a report on research needs on pesticides (Glass, 1976), and newspaper and magazine articles. Finally, we have drawn on the expertise of our own committee members who, as research or extension specialists, are familiar with the problems of developing and registering new chemical pesticides for agricultural and forest uses.

IMPORTANT LEGISLATION DEALING WITH PESTICIDES

A number of important laws enacted since the Federal Food and Drug Act of 1906 regulate the manufacture, distribution, and use of pesticides. The federal laws most directly regulating pesticides are summarized in the Appendix. Additionally, a host of state laws regulates the use of pesticides in the various states. Most of these address certain state and local needs, and some (such as those regulating pesticide applicator registration) are mandated by federal legislation. Stringency of legislation generally has increased with time, especially during the last 10 to 15 years. The burden of proof of safety has shifted from government agencies to the manufacturers and distributors of pesticides. The formation of the Environmental Protection Agency in 1970, and important federal environmental legislation and regulations since that time have enormously increased the cost and complexity of pesticide registration. However, the Federal Pesticide Act of 1978 was an important step in recognition of problems of minor crop uses, conditional pesticide registration, and simplification of registration procedures. These provisions appeared to provide reassurance that government agencies would cooperate in expediting pesticide registration.

DECLINING PRODUCTIVITY OF RESEARCH AND DEVELOPMENT IN THE CHEMICAL PESTICIDE INDUSTRY[1]

Research and development (R&D) expenditures by the U.S. chemical pesticide industry have been expanding in real terms for the past 12 years. Although many new compounds were registered for use in this period, the numbers of new compounds and new uses of existing compounds registered have declined in recent years. In this section we examine data on R&D expenditures to determine whether pesticide innovation also has declined in recent years and, if so, to seek out the explanations for these changes.

Pesticide Research and Development Data

The pesticide industry is a small part of the U.S. chemical industry, and much of its R&D is conducted by divisions of large, diversified chemical and petroleum companies. Therefore, special data from these divisions are needed. This information is available primarily through the National Agricultural Chemicals Association (NACA), an association of pesticide firms. Some information is available from the Environmental Protection Agency. These sources were used in our assessment.

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[1] See also a publication by Eichers (1980).

Past expenditures for R&D obtained from NACA surveys of its member companies are given in Table 1, column 2, in 1972 dollars. R&D has been expanding steadily, as shown in column 3 of this table. Although trends are difficult to identify over such a short period of time, growth of R&D is more rapid in the most recent (15.7 percent for 1976-1978) than in the earliest period (4.9 percent for 1967-1969).

As shown in column 4, Table 1, the dollar value of chemical pesticide sales rose rapidly in the early 1970s, and has risen each year since 1967. The increase reflects price increases, expansion of U.S. agricultural crop acreage, and intensification of pest control activities. Clearly, the market for registered chemical pesticides has been expanding rapidly, and this is one of the main incentives for R&D investments. Available information is insufficient to analyze the sales of new versus older compounds during this period.

The overall level of R&D activity as a percentage of sales is much higher for pesticides than the 2 to 3 percent average for U.S. industry in general (Mansfield, 1968). Although the ratio of R&D expenditures to total sales (Table 1, column 5) is influenced by the long time lags between R&D investments and prospective sales, it seems clear that the ratio of R&D expenditures to sales has been maintained.

R&D expenditures increased in real terms (Table 1), but types of expenditures changed from 1967 through 1978 (Table 2).[2] The percentage of the total R&D investment spent for synthesis, screening, and field testing decreased, while the percentage spent for registration, administration, residue analysis, and environmental testing rose dramatically in recent years. However, funds spent for synthesis and screening also rose in real terms. Although the number of compounds screened for pesticide activity rose between 1967 and 1978, the number of compounds screened per employee declined (Column 4, Table 3).

Table 1. U.S. agricultural research and development expenditures for chemical pesticides for agriculture and forestry based on annual surveys of the National Agricultural Chemicals Association member companies (National Agricultural Chemicals Association, 1978)

Year	Total R&D (mil. $) (1)	Deflated R&D[a] (mil. $) (2)	Growth in R&D (%) (3)	Total chemical pesticide sales[b] (mil. $) (4)	Total R&D ÷ total sales[c] (5)	No. of companies (6)
1967	52.4	66.3		639	8.2	33
1968	56.2	68.1	2.7	691	8.1	33
1969	65.2	75.2	10.4	692	9.4	33
1970	69.9	76.4	1.6	722	9.7	33
1971	87.7	91.4	19.6	1044	8.4	36
1972	98.5	98.5	7.7	1154	8.5	36
1973	110.7	104.5	6.1	1417	7.8	36
1974	134.8	115.8	10.8	1956	6.9	37
1975	160.5	126.1	8.9	2471	6.7	37
1976	219.7	164.1	30.1	2657	7.9	37
1977	250.1	177.0	7.9	3115	8.1	37
1978	289.6	193.3	9.2	3607	8.1	36

[a] Deflated by the 1972 GNP deflator.

[b] Total chemical pesticide sales include foreign and domestic sales and domestic sales from foreign production.

[c] Based only on those companies providing information on total research and development and total sales. This column may not agree with column 1 ÷ column 4.

The proportion of R&D funds spent to support and continue registration of commercial products increased from 13 percent in 1967 to 23 percent in 1970, but declined to 10 percent by 1978 (Column 5, Table 3). Expanding registrations for old products and development of new products consumed an average of 23 and 63 percent of R&D expenditures in recent years, while about 14 percent of expenditures were for continuing registration of compounds in commercial use (National Agricultural Chemicals Association, 1978).

The final two sets of general information are on the amount of time required to register compounds, and annual numbers of new compounds and new use registrations. Both EPA and NACA were able to provide information on these items. Before examining this information one must have some measures of R&D productivity.

Measures of Research and Development Productivity

Productivity of R&D may be measured in several different ways. An important factor in the evaluation is the comparatively long time required to register and develop new chemicals. Bailey (1972) and Grabowski et al. (1978) used new discoveries registered in year "t" divided by average R&D expenditures 4 to 6 years earlier in their economic analyses of the pharmaceutical industry. The number of employees per new product or new use registration, with appropriate time lags, may also be used as a measurement.

In Table 4, four measures of pesticide R&D productivity are given. The first two are expenditures for R&D per new chemical pesticide entity registered based on expenditures that occurred 4 to 6 years earlier. The NACA and EPA information on registered new compounds (Table 5, columns 5 and 6) is used. The third measure is the number of professional R&D employees per new compound, and the fourth is R&D expenditures per new-use registration. Each of the four productivity measures shows 3 years of fairly stable

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[2] Data from NACA surveys are difficult to compare over a period of years. Where known, changes in definitions are noted in footnotes of Tables 1 and 2. However, this information seems to be more complete than that used elsewhere (Lee and Aspelin, 1978; Arthur D. Little, 1975).

Table 2. Percentages of research and development expenditures allocated according to function by American manufacturers of chemical pesticides for agriculture and forestry[a]

Year	Synthesis and screening (1)	Field testing and development[b] (2)	Toxicology and metabolism[c] (3)	Formulation and process development (4)	Registration and administration[d] (5)	Environmental testing and residue analysis[e] (6)
1967	34	30	13	17	5	1
1968	34	31	12	18	5	0
1969	33	31	12	19	5	0
1970	31	32	13	18	6	0
1971	29	33	12	18	5	3
1972	27	34	13	17	5	4
1973	25	34	14	17	5	5
1974	23	29	13	20	11	4
1975	22	29	13	21	10	5
1976	19	23	11	20	11	15
1977	21	20	13	20	10	16
1978	22	20	13	21	9	15

[a] From NACA industry surveys of 33 to 38 companies, 1967 through 1978 (National Agricultural Chemicals Association, 1978).

[b] Does not include residue analysis.

[c] Includes environmental and wildlife toxicology in 1976 through 1978.

[d] Registration only until 1974; administrative costs were included in 1974 and thereafter.

[e] Primarily environmental testing after 1970, and environmental testing and residue analysis in 1976 through 1978. Residue analysis was explicitly listed as a category only in 1976 through 1978. If it existed prior to this time, it may have been distributed among various categories.

Table 3. Professional employees of U.S. manufacturers of chemical pesticides for agriculture and forestry as related to compounds screened and maintenance of pesticide registration[a]

Year	Number of companies (1)	Total prof. employees[b] (2)	Thousands of compounds screened (3)	No. of compounds screened/employee (4)	Percent of R&D for registration maintenance[c] (5)
1967	33	2127	60	28.2	13
1968	33	2234	59	26.4	15
1969	33	2383	61	25.5	18
1970	33	2394	63	26.3	23
1971	36	2504	-[d]	-	17
1972	36	2661	-[d]	-	17
1973	36	2866	-[d]	-	17
1974	37	4191	71	16.9	14
1975	36	4421	85	19.2	13
1976	38	5247	93	17.1	13
1977	38	5120	91	17.1	12
1978	36	5088	84	16.5	10

[a] From NACA industry surveys of 33 to 38 companies, 1967 through 1978 (National Agricultural Chemicals Association, 1978).

[b] After 1973 the figure includes employees at non-U.S. locations.

[c] Companies were asked what percent of their R&D expenditures was for maintenance of registration of existing products.

[d] Not available.

Table 4. Productivity measures for research and development for U.S. manufacturers of chemical pesticides for agriculture and forestry, 1973-1978

Year	R&D expenditure per new chemical pesticide entity[a]		R&D employee years per new chemical pesticide entity (EPA)[b] (3)	R&D expenditures per new-use registration (EPA)[bc] (thousand $) (4)
	NACA (mil. $) (1)	EPA[b] (mil. $) (2)		
1973	9.98	9.98	321.1	18.47
1974	9.15	9.15	292.1	26.12
1975	8.10	8.10	242.7	28.42
1976	22.19	12.68	356.9	46.11
1977	32.71	49.01	1338.5	134.24
1978	53.13	35.42	1079.7	236.16

[a] Based on the deflated R&D expenditures of column 2, Table 1. R&D expenditures are average values for 4 to 6 years earlier. The numbers of new chemical pesticide entities are from columns 5 and 6 in Table 5. The number of new chemical pesticide entities assumed for 1973 in column 1 is 7, the same as the number (from column 6 in Table 5) used in calculating column 2.

[b] EPA values for new chemical pesticide entities were corrected for the reporting period as indicated in footnote *c*, Table 5. EPA data were derived from the National Academy of Sciences (1975), President's Science Advisory Committee, Panel on Chemicals and Health (1973), and Aspelin (1979).

[c] EPA new-use registrations were adjusted for the fiscal year time change.

Table 5. Time required for registration, and number of new registrations of chemical pesticides for agriculture and forestry, 1967-1978[a]

Year	Registration time for new products, NACA data		Registration time for new products and new uses, EPA data		New chemical pesticide entities		New-use registrations (EPA)[e] (number) (7)
	Submission to approval (months) (1)	Discovery to market (months) (2)	Total time (months) (3)	Agency review (months) (4)	NACA (number) (5)	EPA[c] (number) (6)	
1967	7[b]	60[b]			8	9	
1968					12	9	
1969	18[c]	70[c]			10	9	3,437
1970	11	77			11	3	1,029
1971						1	1,662
1972						7	3,077
1973	22	80				7	3,784
1974	18	97	9	3.2	8	8[d]	2,304
1975	14	93			10	10[d]	2,850
1976	14	74			4	7	1,925[d]
1977	29	110	19	7.2	3	2	730[d]
1978	32	69			2	3	450

[a] National Agricultural Chemicals Association (NACA) (1978) data are from industry surveys of 33 to 38 companies. EPA data are from President's Science Advisory Committee, Panel on Chemicals and Health (1973), National Academy of Sciences (1975), and Aspelin (1979).

[b] Average for 1963 through 1967.

[c] Average for 1967 through 1971.

[d] Figures listed are adjusted for change in reporting time.

[e] Fiscal year accounting.

output and then a rapid increase in expenditures per unit of discovery and registration. Expenditures and employees per new discovery actually fell in the mid-1970s before rising rapidly. The decline in R&D productivity for new compounds is observed in only the last 3 years. Because the numbers are very large, it appears certain that pesticide R&D productivity has declined rapidly in terms of both new compounds and new formulations or new uses of existing compounds.

There is some indication that the 1978 amendments to FIFRA which allow "conditional pesticide registrations" may have reversed the recent downward trend in registrations. Preliminary indications are that six or seven compounds were registered by EPA in calendar year 1979. If this estimate is correct, productivity for 1979 would be expected to improve according to the EPA figures (Table 5) and assumed rates of R&D expansion.

Alternative Explanations of the Productivity Decline

Several possible reasons are given in other studies for declines in chemical R&D effectiveness. Among those relevant to pesticides are: (a) measurement problems, (b) depletion of the stock of potentially discoverable pesticide compounds, (c) reduced demand for chemical pesticides, and (d) increased stringency of government regulations. These explanations will be examined in turn to see if items *a* through *c* explain the declines observed in Table 4. Finally, various measures of government regulatory stringency will be compared with the numbers of new pesticides discovered and registered for use in recent years.

Measurement Problems

One important measurement problem is how to determine which new compounds are agricultural and forest pesticides. Different definitions lead to different numbers of registrations. The EPA figures for new chemical pesticide entities registered from 1967 through 1974, as given by the National Academy of Sciences (1975), differ from data published by the NACA (Table 5). Another type of measurement problem is that the number of new compounds registered by EPA may not be an adequate measure of R&D output in that the number may not reflect the spectrum of pesticidal activity or the potential sales. Conceivably, a given registration may have a much more significant impact on sales volume and pest control than most products registered previously. This may be true also for new use registrations. EPA, industry, and pest-management researchers agree that only major-pest, major-crop registrations are being sought at present. Because new registrations require very large inputs of time and expense, more and more crops are being added to the so-called "minor-use" category (pesticides for use on minor crops or for minor uses on major crops).

New, potentially useful processes and development also may be discovered, which are not measured by numbers of products registered. Additionally, new uses for pesticides frequently are found after a pesticide is registered, but registration for these new uses is not pursued because the return would be too small. The Federal Pesticide Act of 1978 provides for use of a registered product to control a pest not specified on the label, but such additional uses cannot be recommended by extension personnel or farm advisers under current regulations.

Depletion

The depletion explanation for declining R&D productivity is that, as the search process proceeds, discovery of new pesticides becomes more difficult. This process was found to be a significant factor in declining returns to pharmaceutical R&D in both the United States (Bailey, 1972) and Great Britain (Grabowski et al., 1978).

Discovery and registration of new pesticides appear not to be declining worldwide. Although little information is available on registration of pesticides in foreign countries, *Farm Chemicals* magazine (Anonymous, 1978) surveyed "leading producers from the U.S., Europe and Japan." In 1976 and 1977, seven new agricultural compounds were registered in the United States, but 19 new compounds were registered in other countries. *Farm Chemicals* reported also that foreign companies screened approximately 5400 compounds per company, while U.S. companies screened an average of about 3000 compounds per company in recent years. Moreover, in comparison with pesticide firms in the United States, foreign companies appear to be devoting a larger share of R&D expenditures to product expansion and maintenance of existing products than for new product development. Of approximately 180 commercial herbicides available in the world, at least 30 are not registered for use in the United States according to our information.

According to the preceding evidence, depletion of the stock of potentially beneficial compounds does not seem to be a major hindrance to R&D productivity. More research is needed to document the timing of discovery, commercial importance, and degree of duplication of compounds used in foreign countries compared with pesticides registered in the United States. However, the threat that other nations may surpass the United States in developing new agricultural chemicals looms larger as regulation becomes relatively more stringent in the United States.

Demand for Pesticides

In general, U.S. pesticide sales seem to be expanding (see Table 1, column 4). As an EPA report states (Lee and Aspelin, 1978): "The U.S. pesticide producing industry is a growth industry based on the past record, and is expected to be in the future as well." The number of firms registered for the first time with EPA as a pesticide manufacturer remained steady in recent years. Values of agricultural and forest products to be protected are increasing. A statistical analysis of the data in Table 1 suggests that pesticide firms expand R&D investment following years of high pesticide sales. Each of these factors indicates a steady or growing demand for pesticides and pesticide investments. However, the growth in demand does not preclude the possibility that regulation or one of the other factors has slowed pesticide innovation from a given level of R&D. Also, investments in R&D might have been higher with less regulation.

Regulatory Stringency

The effect of regulatory stringency can be examined in several ways. As a measure of regulatory stringency in the pharmaceutical industry, Bailey (1972) used the coincidence of the timing of legislative changes with productivity declines, while Grabowski et al. (1978) used the months of delay from new drug submission to approval. Delay time is especially important to R&D rate-of-return computations. Regulatory impact may be measured also by levels of R&D expenditures and shifts among functions and types of products (Table 2).

As indicated elsewhere, major changes in pesticide legislation and registration occurred in 1947, 1970, 1972, and 1978. EPA assumed the registration responsibility in 1970, and changes in FIFRA were made in 1972 and 1978. We examine here the R&D expenditures and registration responses for 1971, 1973, and 1979 for evidence of effects of the changes that occurred in 1970, 1972, and 1978. Other effects of the changes in legislation and regulation might not surface for years but would be difficult to isolate because of the possible influence of other factors on investment.

The numbers of registrations of new chemical pesticide entities and of new uses seem to have decreased substantially following the movement of registrations from USDA to EPA in 1970 and 1971 (Columns 6 and 7, Table 5). Following the 1972 amendments that required reregistration of all pesticides there was an increase in new-use registrations. Preliminary indications are that the 1978 amendments may have helped to increase new-entity registrations during 1979.

Industry R&D investment response to pesticide legislation is mixed. The year 1970 was a period of very low investment, but in 1971 R&D investment expanded at the highest rate during the 1967 to 1975 period (Table 1). In 1973, following the 1972 FIFRA amendments, R&D expansion was the smallest since 1970, but the slow-down was temporary.

Perhaps a more direct measure of EPA regulatory stringency is the time required for pesticide registration approval (Table 5). EPA and NACA data are divergent, in part because EPA figures show registration times for new products and registered new uses, whereas NACA data include only new products. There is much year-to-year variation in these delay times. However, for the past 12 years the trend is to longer periods of time for all phases of testing and approval. EPA sources (Lee and Aspelin, 1978) indicate that in 1977 only about 7 of 19 months required for registration (Table 5) involved agency review time, but this claim is disputed by industry sources (National Agricultural Chemicals Association, 1978).

The delay time involved under alternative regulatory schemes is uncertain. The reduced efficacy testing requirements of the 1978 amendments to FIFRA probably will not reduce efficacy testing needed for company investment decisions. Delay times and levels of pesticide industry R&D expenditures the following year are difficult to interpret. Funds spent to generate additional data required for registration might be offset in part by less investment in the search for new compounds. Clearly, the increased delay times in 1977 and 1978 are concurrent with the greatest R&D expenditures per unit of output as shown in Table 4.

The final indication of regulatory impacts on R&D expenditures is the shift in uses of R&D funds. In the functional division of expenditures for the NACA member companies (Table 2), the most striking feature is the decline through time of the share of funds devoted to innovative or discovery activities. Synthesis, screening, and field testing (Columns 1 and 2) show a sizeable decline from about 65 percent of R&D expenditures in the late 1960s to about 42 percent in the late 1970s. There has been a slight increase in expenditures for formulation and process development. The most sizeable expenditure gains are in registration and administration, environmental testing, and residue analysis. The combined total was 6 percent or less prior to 1971 and 24 to 27 percent since 1975. This increase can be attributed to a combination of increased public concern and increased stringency of the regulatory regimes.

Some pesticide R&D expenditures are difficult to categorize. In recent years, new categories such as residue analysis, environmental chemistry, and other expenditures have claimed an increasing share of expenditures. Regulations and additional testing requirements contributed to the expansion of expenditures in this area (Lee and Aspelin, 1978, p. 34). Part of the increase in testing costs is due to the recent rapid increase in cost of laboratory animal studies. Private laboratory estimates of per-test costs have risen about seven-fold in the 1973 to 1979 period, largely because salaries of pathologists and toxicologists increased 25 to 40 percent in 2 to 3 years, and laboratory practices have become substantially more complex (for example, more tissues must be examined). EPA (Johnson, 1978) estimates the average cost of a chronic feeding study to be $150,000. A 1978 private laboratory estimate is $150,000 for a mouse test and $230,000 for a rat test

(Ruttan et al., 1980).

Under FIFRA, EPA is responsible for putting its data requirements for registration in written form. Guidelines for registering pesticides were proposed by EPA in July 1978 (Fowler, 1978), and an economic impact analysis of the guidelines was published on September 6, 1978 (Johnson, 1978). The guidelines add certainty to testing requirements in the future. The EPA economic analysis estimated future registration costs by tabulating expected costs for: (a) incremental cost of guidelines (new tests and laboratory practices), (b) the cost of submitting data to meet current standards, and (c) the value in current prices of acceptable data already submitted to EPA in support of a registration. The latter two items pertain to reregistration only, while the first item is for new registrations. The EPA estimate for the cost of registration for an "average" new compound is about $390,000.[3]

FMC Corporation (1978) has prepared a rebuttal to the EPA economic analysis. FMC's analysis contends that two major difficulties are present in the EPA analysis. First, FMC's "average" product is a high-volume product which requires more extensive testing than does EPA's average product. Second, testing costs per new ingredient, particularly in the product chemistry and the human domestic hazard category, are underestimated by EPA. Both the number of tests required and the cost per test are estimated to be higher by FMC than by EPA.[4] The FMC cost figures are $1.3 million for the "average" EPA product and $2.9 million for the "average" FMC product.

In Brief

This evaluation indicates that there is some possibility that depletion and emphasis on pesticides with potentially large sales volume may explain some of the recent rise in costs per new pesticide registered. But the rise in safety testing costs and registration delay times in 1977-1978 occurred at the same time as the rise in costs per pesticide approved. The shift of resources from discovery activities to safety testing has decreased the number of compounds screened. All of this has been taking place in a rapidly expanding pesticide sales environment. The private benefit of getting a new compound approved is very high, but the probability of a success is falling, and costs of new compound development are rising rapidly. Whether or not the conditional registration and efficacy testing waivers of the 1978 FIFRA amendments can offset these increased regulatory costs will be critical for the next few years.

ADDITIONAL IMPACTS OF PESTICIDE REGULATION

Examination of the effects of government regulation on innovation in the pesticide industry projects an image of an industry grappling with sharply higher costs of development, but one in which industry seems to be coping with the problem by passing increased costs on to the user and consumer. Increased cost of chemical pesticides that will be passed on in the form of higher prices to consumers is one obvious impact of government regulation. There are ~~other, more~~ subtle but perhaps more harmful costs that must be considered in the overall evaluation.

Diversion of Effort of Scientists in the Public Sector

Scientists at the agricultural experiment stations in various states and in the U.S. Department of Agriculture are involved in the development of new chemical pesticides for agricultural and forest uses. However, developing these new chemicals is only a small part of the total research effort at these institutions. One recent effect of increasing government regulation has been to increase the amount of time these publicly supported scientists must allocate to defending needed agricultural chemicals and to making adjustments in pest control practices as important chemicals are removed from the marketplace or are restricted in use patterns. These and other scientists also must respond to government requests for information, train pesticide applicators, assist in obtaining information needed for registration, make residue analyses, and perform many other pesticide-related activities. Although some of the required investigations would be done as a part of comprehensive research on pesticides, a substantial portion must be diverted from other needed areas of research.

In an attempt to obtain some understanding of the impact of regulations on university research, extension, and teaching, we examined the repercussions of the Federal Environmental Pesticide Control Act of 1972

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[3] An "average" product is typical in terms of volume and range of uses across crops, locations, and target pests.

[4] According to FMC, its average chronic feeding study cost $420,000, compared with the private laboratory estimate of only $150,000 for a mouse test and $230,000 for a rat test.

(FEPCA, amended FIFRA) from 1972 to 1978 in the New York State College of Agriculture and Life Sciences at Cornell University (including the agricultural experiment stations at Ithaca and Geneva and Cooperative Extension). This law, more than any other, has placed additional responsibilities on plant protection scientists. Some of the more relevant features of FEPCA in this regard include: (1) establishment of new intrastate and interstate requirements for registration of all pesticides, (2) classification of pesticides for general or restricted use and training and certification of those who use restricted materials, (3) state registration of pesticides under certain circumstances (section 24c), (4) emergency exemptions from normal registration procedures (section 18), and (5) establishment of an RPAR (rebuttable presumption against registration) system for determining whether a pesticide's registration or reregistration would cause unreasonable adverse effects on the environment.

The most dramatic change since the enactment of FEPCA has been the increase in faculty and administrative effort in behalf of minor crops, section 18 and section 24c registrations, and the National Agricultural Pesticide Impact Assessment Program as part of the RPAR process. Many faculty members currently spend 3 days per month on pesticide registration activities, or 15% of their total effort. During the 1972-1978 period, a total of one scientist-year was devoted strictly to section 18, section 24c, and RPAR affairs. In the same period, a total of 6.8 years of work was accumulated by technical and clerical staff hired largely to facilitate work in this area. The total administrative time required per year for pesticide regulatory matters has more than doubled since 1972.

Extension education carries the heaviest workload for registration requirements. Faculty members whose responsibilities are entirely or predominantly in extension are most severely affected. Moreover, faculty efforts in behalf of pesticide registration often receive less than adequate recognition from university administrators. Sometimes, therefore, motivation may be a problem for those who must carry the load for pesticide regulatory matters. In an environment where research resources have not been expanding there is considerable competition for faculty members' efforts. If current regulatory demands continue, more resources are needed for RPAR activities.

Certification of restricted pesticide users and associated training programs have had the second largest impact. The simple exercise of preparing and administering examinations consumed about 1.2 years of scientist and supporting staff time during the 1972-1978 period. Another year was accumulated by college staff who toured the state presenting training sessions, but this could be justified as normal extension duty. Preparation of certification manuals, preparation of training aids, and legislative liaison work have required about 7 scientist-years and 9 staff-years of effort.

A survey of faculty research full-time equivalents spent on chemical control of insects, pathogens, and weeds indicated very little change from 1972 to 1978. During the same time, there was about a 10% increase in efforts on nonchemical control of pests. However, the technical support which assisted these research programs showed a 15% decrease for chemical control and a 100% increase in nonchemical control. The number of chemicals tested for efficacy, residues, and yield was similar in 1972 and 1978. However, no distinction was made between the number of new chemicals tested and the number of old chemicals tested for new uses.

The impact of FEPCA on teaching programs has been small, although regulatory history, pesticide certification, pesticide safety, and registration requirements formed a part of at least seven courses. The time involved has increased substantially since 1972 and amounted to part of a lecture in some courses to five full class periods in one course.[5]

Although these data are very limited and insufficient to draw extensive conclusions, indications are that during the 1972-1978 period a total of at least 10 scientist-years and 16 support-years was spent at the New York State College of Agriculture and Life Sciences on regulations imposed by FEPCA. A similar survey of the South Carolina Agricultural Experiment Station, Clemson University, revealed similar impacts on faculty and staff resources.

Some states are affected more than others by regulatory-related activities. If the two institutions surveyed represent an average rather than the exception, however, at least 500 scientist years may have been diverted to regulatory-related activities at state experiment stations in the United States during 1972-1978. These surveys do not include estimates of the amount of research time that is devoted to subjects inspired by regulatory concerns. We have not been able to estimate the magnitude of the diversion of USDA scientists.

The influence on agricultural productivity resulting from the recent diversion of scientific effort to regulatory activities has probably been relatively small to date because the major innovations that increase agricultural productivity generally require more than 10 years from conception to extensive implementation. In the long run, however, the diversion of scientific effort to regulatory activities will be very costly to the U.S. public. The reasons are that, in addition to paying the cost of the regulatory activities, the public will lose the benefits of the scientific output that would otherwise result. The annual rate of return to the U.S. public from investment in agricultural research is approximately 50% (Evenson et al., 1979).

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[5] In some institutions, new curricula are being offered in pest management.

Effects of RPAR on Pesticide Use Patterns

The "rebuttable presumption against registration" (RPAR) procedure was developed to review thoroughly the status of agricultural chemicals that might have potential for serious harm to humans or the environment as a basis for determining whether registration of those chemicals should continue. We have reviewed some of the effects of this procedure in the preceding pages. Also, we have noted the demands that this procedure places upon state experiment station scientists.

When a chemical pesticide is removed from the market or when its use is severely restricted, one effect is the substitution of older, less effective chemicals if these are available. These substitutes often must be used in greater volume because more pesticide is required to obtain equivalent pest control. Therefore, the overall effect may be to increase the volume of pesticide used.

An important example is the recent decision of the Environmental Protection Agency to suspend the registration of 1,2-dibromo-3-chloropropane (DBCP)[6] for health and safety reasons for all nematicide uses except for nematodes on pineapple. Replacements for DBCP as a preplant treatment on peaches on the East Coast will require four to seven times as much material for equivalent control (Table 6). If ethyl-4-(methylthio)-*m*-tolyl-isopropylphosphoramidate (fenamiphos) is approved for use on peaches, the amount of active material per acre per application will be less than that of DBCP; however, fenamiphos will require annual application (DBCP is applied biennially), and it is less effective than DBCP for control of ring nematodes.

The cost of treatment ($27-$45 per acre for DBCP in 1974 — Table 6) was modest relative to gains realized in terms of expanded productivity and prolonged tree life. During the 5-year period from 1974 to 1979, the retail prices of fumigants increased two to four times. However, because of the loss of DBCP, the cost increase of *preplant* treatments was even greater — from $27-$45 per acre in 1974 to $125 or more in 1979. Some of this increase was due to inflation and some to rising prices of petroleum, but a substantial fraction represented the cost of regulation being passed on to farmers. In this instance, more material is needed at greater cost, with less effective nematode control and greater expenditure of energy in the more frequent application of treatments. Additionally, the hazard to applicators is increased because of the more frequent applications of alternative nematicides required to provide control.

The use of DBCP was suspended also for established citrus, deciduous fruits, and vines, which are important in the West. DBCP was used no more frequently than once in 3 years for citrus, whereas the potential alternative nematicide must be applied annually. No nematicide or cultural practice now available is as effective as DBCP for prolonging the life of groves and vineyards. Unpublished studies by the California Department of Food and Agriculture indicate that, with suitable precautions, DBCP can be applied without hazard to workers, but the Department considers that it is unlikely to pursue further the use of DBCP because traces of the compound have been found in certain well waters.

Most agricultural scientists are pleased to cooperate with federal regulatory agencies in their requests for information and consider it a part of their responsibility to the general public. However, agricultural scientists have at times been made to feel that they were wasting their time by such cooperation. Some recent actions of EPA reinforce the widespread belief that facts developed from careful scientific investigation are often not heeded when regulatory decisions are made.

For example, the costly and tedious RPAR process may be triggered on the basis of tenuous information or poorly performed experiments, and, when decisions are made, the findings in the RPAR process may be ignored

Table 6. Per acre material costs of nematode control on peach trees in 1974 and 1979 with selected chemicals used in South Carolina

Chemical and rate of formulated product per acre	Treatment mode	Material cost per acre[a]	
		1974	1979
DBCP (3-5 gallons)[b]	Preplant and postplant	$27- 45	$ 79-115
Ethylene dibromide (12-20 gallons)	Preplant	84-140	140-200
1,3-dichloropropene (21-35 gallons)	Preplant	35- 50	125-210
Fenamiphos 15G (60-100 lb)[c]	Preplant and postplant		100-165

[a] Cost is variable depending on soil type and whether broadcast or strip treatments are used.

[b] Registration of DBCP was suspended in November 1979.

[c] Not currently registered for use on peaches; has potential for postplant treatments.

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[6] DBCP was widely used as a nematicide because it was very effective at low rates, was reasonably priced, and was of low toxicity to plants. It was used as a preplant treatment for some crops and was the only chemical in the fumigant class that was available for use on established crops such as peaches, pineapple, and additional fruits and nuts.

in favor of information that is scientifically indefensible. In the recent EPA decision to suspend selected usages of the herbicide 2,4,5-T, carefully developed studies made as part of EPA's RPAR process (USDA, 1979) were ignored. Instead, EPA relied on a retrospective epidemiological study it conducted in a forested area in Oregon where certain women claimed that use of 2,4,5-T in forest management was a cause of an excessive number of spontaneous abortions. In the 6-year period included in the study, 2,4,5-T was used in significant quantities in 30 months, but EPA claimed a significant increase in the rate of spontaneous abortions in only 1 month. A subsequent examination of EPA's data (Newton, 1979) showed that in this month there were ten cases, but in eight of these the women involved were from areas in which there was no known use of 2,4,5-T during the entire 6-year period. The EPA study was reviewed by Health and Welfare Canada and Agriculture Canada, and, on April 19, 1979, they stated, "The recently released reports that prompted the U.S. decision appear to be inadequate to support the regulatory action taken." The Department of Public Health, Division of Public Health, New Zealand (1979), reached a similar conclusion. This and additional evidence was reviewed by Crosby et al. (1979). EPA's own Scientific Advisory Panel to the Federal Insecticide, Fungicide, and Rodenticide Act recommended that no hearing be held for the registered uses of 2,4,5-T because "no evidence of an immediate or substantial hazard to human health or the environment" was found (Torgeson et al., 1979). In the legal arena, a U.S. District Court upheld the suspension decision, but explained that "the Court is not empowered to substitute its judgment for that of the EPA," adding that "...the Court will frankly concede that it arrives at this decision with great reluctance and would not in its judgment have ordered the emergency suspensions on the basis of the information before the EPA" (Harvey, 1979). Nonetheless, EPA still does not admit that it acted on invalid evidence (Johnson, 1980) and persists in its emergency suspension of 2,4,5-T.

Integrated Pest Management

Integrated pest management (IPM) involves the integrated use of all applicable pest control principles and practices. IPM includes the use of chemical pesticides, but only as they are needed, and with management of their application to limit the harm done to beneficial organisms. Frequently this requires pesticides that are selective for the target pest. The property of a narrow spectrum of pesticidal activity necessarily limits the numbers of uses of a pesticide to one or a few crops and to one or a few pests.

One of the most important and far-reaching effects of spiraling costs of developing new chemical pesticides is the effect on chemicals having a narrow spectrum of activity. In most instances, costs to industry do not justify the development of such chemicals. This situation restricts the development of IPM systems now for minor crops, and it may eventually have severely restrictive effects on IPM systems for crops of large acreages as well.

A major research objective is to reduce pesticide use. There are several approaches. One is to search for new compounds that are effective at lower rates of application. This approach reduces the volume of pesticide applied to a crop — a practice which reduces cost and residues. Another is to combine pesticide use with other pest control practices, or to eliminate pesticides altogether. A third is to investigate the biology of pests and its interaction with pest control measures so that the most effective control practices can be applied at the most opportune time. A fourth is to develop pest resistant crop varieties that require less help from pesticides and other control practices.

Government regulations may have important impacts on attempts to reduce overall pesticide usage. This point is well illustrated by a report which our committee received from Dr. D. L. Kittock, a colleague formerly in the U.S. Department of Agriculture, who is now retired. The following is quoted from this report:

> We have been working on chemical termination of cotton for control of pink bollworm for 8 years. This involves treating cotton plants in the fall with a single application of a relatively non-toxic plant growth regulator or mixture of two plant growth regulators to stop fruiting. If the application is properly timed, we prevent formation of bolls that will not mature before frost, but do not affect those that will mature. The lack of immature bolls in the fall denies the overwintering generation of pink bollworm's food source and habitat. We have been able to reduce the overwintering generation of pink bollworm 90 to 95% by use of chemical termination with little or no effect on lint yield. This should delay population build-up the following summer by at least one generation which is about 30 days or five insecticide applications. We have not been able to adequately test the effects of chemical termination on pink bollworm population the season following treatment. In order to do so it will require treatment of several thousand acres in an isolated area because of the pink bollworm moth's ability to fly long distances and reinfest fields. Treatment of a large acreage will require obtaining an experimental label with allowable tolerances on at least one suitable plant growth regulator.
>
> We have identified four plant growth regulators that are fast acting and effective for chemical termination. They are: (1) 2,4-D at 1 pound/40 acres, (2) dicamba at 1 pound/20 acres, (3) silvex at 1 pound/20 acres, and (4) Pennwalt's TD-1123 at 1 pound/acre. We have ruled out use of 2,4-D because it severely reduces germination and emergence of seed and makes leaves, flowers, and squares stick, which presumably adds to the dust problem under attack by OSHA. Silvex was ruled out by EPA this spring. We had hoped to get an experimental label on dicamba with tolerance this year. However, in recent conversation with Velsicol Corp., we found that they do not wish to pursue registration of dicamba. Last Friday, I was told Pennwalt had decided to discontinue development of TD-1123.

> Government regulations affected only silvex directly. However, government regulations inhibited Velsicol and Pennwalt because of the high cost of testing that is required for registration.
>
> The economic and environmental cost of these decisions could be quite high. One-half of all insecticide use in the U.S. is by agriculture. One-half of that (25% of the total) is used on cotton. Chemical termination theoretically should be as effective for control of boll weevil as well as pink bollworm. Therefore, under best possible results it might reduce insecticide use on cotton up to 80% or a 20% reduction of total U.S. insecticide use. Of course, it is possible that the technique may not work at all on a field scale. Most likely the technique will have some value and reduce insecticide use somewhere between 0 and 20%. We may never know if we can't test the concept.

Other examples could be cited. New bactericides to replace streptomycin and oxytetracycline which are used to control bacterial diseases of plants are not being developed because of prohibitive costs. Concerns have mounted about the use of antibiotics such as streptomycin and oxytetracycline for plant disease control because of fears that resistance to these chemicals might be transmitted to pathogens of humans and animals. The lack of alternatives to these antibiotics is a matter of serious concern to plant pathologists and farmers.

The problems just described are similar to those encountered with so-called "minor uses" of chemical pesticides on crops of limited value or acreage and on major crops for pest control needs which are significant only in limited areas. The problem of minor uses was the subject of another CAST Report (Upchurch et al., 1977). The Federal Pesticide Act of 1978 was an important step forward in dealing with the minor use problem, and, if fully implemented, will help to alleviate some of the problems in innovation that hinder development of pesticides needed to support IPM. The provisions of this law for conditional registration and data requirements for minor use pesticides will be especially helpful if regulations are implemented to encourage the registration of pesticides that have a narrow spectrum of activity. Cooperation of federal and state agencies in granting tolerances for emergency uses under section 18 provisions and in developing state registrations under section 24c provisions also would be very helpful in solving these problems.

Biological Control

Biological control means the use of biological agents to control pests. It is not necessarily nonchemical in nature, because some biological control agents are chemicals produced biologically. There are several classes of biological control agents.

Parasites and predators are living organisms that attack and destroy pests. They include microorganisms such as bacteria, viruses, nematodes, or fungi, but they may be larger living organisms such as parasitic wasps, beetles, or birds.

Antagonists may control pests by secreting biologically active compounds which are inhibitory. For example, marigolds secrete substances which inhibit certain nematodes. The crown gall disease of woody and herbaceous plants may sometimes be controlled by a bacterium that is antagonistic to the bacterium causing crown gall.

Sex pheromones are chemicals that may be used to disrupt mating patterns of insects. Resistance mechanisms sometimes can be utilized through genetic manipulation to increase the natural resistance of plants to pests.

Biological control agents are valuable in overall pest control strategy. Like chemical pesticides, however, they have limitations. They are generally more difficult to develop and use than are chemical pesticides. As is true of chemical pesticides, biological control agents may lose effectiveness with time because the pests develop resistance to them. Although nonliving chemical biological control agents disappear from the environment, like chemical pesticides, this is not necessarily true of living biological control agents. Depending on the organism and the circumstances under which it is used, living biological control agents may persist longer in the environment than do chemical pesticides, and they are more difficult to eliminate if their presence is found harmful. In fact, living biological agents may increase in the environment.

How do government regulations affect innovation in biological control? Until recently, agents for biological control were required to undergo the same kinds of tests that were required for new pesticides. However, current federal regulations (Jellinek, 1979) do not restrict the movement of parasites and predators within the United States. Movement from outside the United States is subject to quarantine laws, but registration as a pesticide is not required. The movement of antagonistic microbes within the United States is not restricted unless the microbes are classified as pests. However, sex attractants and other types of chemicals produced by biological agents are subject to pesticide regulations. Since most chemicals of this nature are specific in their activity, their commercial development is not financially attractive at present. At least one source (Tucker, 1978) indicates that federal regulations have already prevented the development of certain biological agents, such as juvenile hormones and parasitic microbes, for insect control. Liberalized regulations for biological agents in the natural environment which might be developed for biological control are being studied.

Technological Leadership

Agricultural scientists who test new pesticides have noticed that the proportion of new test chemicals originating from outside the United States is increasing. This may not be a matter of serious concern, but it raises certain troubling questions. Are chemical manufacturers finding costs of developing agricultural chemicals outside the United States low enough to focus on the market abroad rather than on the United States? Is it becoming more attractive to market new chemicals abroad before undertaking development of them in the United States? If so, American farmers might find themselves at a significant disadvantage in pest control compared with farmers in other countries. Could the technology to discover and develop chemicals for biological control and integrated pest management flourish abroad while being restricted in the United States? There are indications that advances in pesticide innovation in the United States may be lagging behind those of other developed nations (Anonymous, 1978).

CONCLUDING REMARKS

Increasingly stringent regulation of agricultural chemicals in recent years has required private industry to verify the safety of both new and old chemical pesticides. This procedure is very expensive. Generally, industry has been able to pass on part or all of these costs of regulation to users. Costs of regulation do not appear to have greatly inhibited the search for new compounds, but some research and development funds have been diverted from synthesis, screening, and field testing to other activities (Table 2). However, the effects in agriculture are not uniform. One effect has been to encourage the development of chemical pesticides having a broad spectrum of activity at the expense of compounds with more specific activity that would be useful in IPM.

If current trends in regulation continue, one long-term effect will probably be reduced respect for pesticide regulations among users. If, for instance, the trend continues toward registration of broad-spectrum chemical pesticides on major crops only, the temptation to engage in illegal use of pesticides will increase. Farmers and gardeners confronted daily with pest control problems will become less concerned with use of chemicals in accordance with label directions if they know that the chemicals will work for crops not on the label, especially if they believe that label restrictions are based on economic reasons rather than safety considerations. Vigorous implementation of the "minor use" and conditional registration provisions in the Federal Pesticide Act of 1978 would help to overcome this problem.

The Federal Pesticide Act of 1978 contains a number of provisions for registration and use of pesticides which are helpful to agricultural, forest, and business interests. Wise use of this law by all parties involved in the registration, production, and use of pesticides would go far toward alleviating many difficult problems associated with pesticides.

Certain important issues relating to government regulation have not been addressed in this review. Some of them defy attempts at a complete assessment because of their complexity and lack of reliable data; nevertheless, they should be kept in the public view because they are very important. Examples of questions that are of concern in analyses of regulations are these:

1. What is the impact of substituting a highly toxic, nonpersistent chemical pesticide (such as parathion) for a persistent chemical pesticide of low mammalian toxicity (such as DDT) or vice versa? How is the hazard of the former to humans evaluated against the hazard of the latter to the environment?
2. Is development of safer, more effective chemical pesticides unduly inhibited by existing regulations? Do current regulatory activities overemphasize the regulatory process and underemphasize the objectives of regulation?
3. Is chemical pesticide use increasing or decreasing as a result of government regulation? Some uses seem to be increasing as a result of government regulation.
4. Would less government regulation spur the development of safer, more effective pesticides, or would the effect be injurious to humans and the environment?
5. Are the costs of government regulation to industry, agriculture, and forestry, and eventually the consumer, justified by the benefits obtained? How can risks of pesticide manufacture and use be balanced against the risks of regulation?
6. What incentives are needed to bring about more effective collaboration among the several public and private institutions involved in pesticide research, production, and regulation?

An assessment of the impacts of government regulation on the development and use of agricultural chemicals is not complete unless long-term effects are considered. Answers to these questions will become clearer as time progresses.

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APPENDIX

The Federal Food and Drug Act of 1906

Generally referred to as the Pure Food Act, this law was designed to prohibit the use in food of chemicals known to be harmful to humans. Under this law the burden of proof of the harmful or poisonous effect of any chemical rested with the Food and Drug Administration (formerly the Bureau of Chemistry).

The Federal Insecticide Act of 1910

An act for preventing the manufacture, sale, or transportation of adulterated or misbranded insecticides and fungicides, for regulating traffic thereof, and for other purposes.

The Federal Food, Drug and Cosmetic Act of 1938

This act was passed by Congress on June 25, 1938, and became effective one year later. It superseded the 1906 Food and Drug Act.

It prohibited the unnecessary addition of poisonous substances to food and set forth the procedures for establishing tolerances for instances in which such substances could be used without endangering human health. No tolerance could be established unless the chemical in question could be used in such a way that the public health would be protected.

Under this Act the Food and Drug Administration could not bar the use of a chemical unless it could prove that the chemical was harmful. Hearings were held in 1944 and 1950 for the purpose of establishing tolerances. All chemicals and tolerances established by these hearings were for fruits and vegetables.

This Act provided that tolerances be established for pesticide residues in foods where these materials were necessary for the protection of the food supply.

The Federal Insecticide, Fungicide and Rodenticide Act of 1947 (FIFRA)

This Act was passed on June 15, 1947, and became effective one year later.

It superseded the Insecticide Act of 1910 and extended coverage to include herbicides and rodenticides.

It further established regulations relating to the certification of the usefulness of chemicals in agriculture and required registration of all compounds with the Secretary of Agriculture. A tolerance or exemption from a tolerance continued to be requested under the provisions of the 1938 Food, Drug and Cosmetic Act.

The 1947 FIFRA placed the responsibility for registration with the manufacturer. It specified requirements for safety precautions in applying and handling agricultural chemicals and required requests for continued registration on a 5-year basis.

The Act provided that all material sold in interstate commerce must be correctly labeled and that the label must be registered and approved by the USDA.

It also provided penalties for misbranding and unregistered uses being recommended on the labels.

Public Law 518

Also called the "Miller Amendment" or the "Miller Pesticide Residue Amendment."

Public Law 518, the Miller Amendment to the Food, Drug, and Cosmetic Act, was passed July 22, 1954, and provided that any raw agricultural commodity may be condemned as adulterated if it contains any pesticide chemical whose safety has not been formally cleared, or which is present in amounts exceeding established tolerances.

This law places the responsibility on the manufacturer for clearing all legal requirements for use of agricultural chemicals with the USDA and the FDA.

It requires that a specific tolerance be established for each use to be made of any chemical, or the establishment of an exemption from a tolerance where exemptions can be justified.

It gives the Secretary of Health, Education and Welfare the power to establish such residue tolerances and spells out in detail the procedure to be followed.

It further requires each product to carry on the label full and specific instructions for use so as to meet the legal residue tolerances specified by the Food and Drug Administration.

The Department of Agriculture enters the picture to certify that the chemical is useful for the production of the crop in question, and that the tolerance proposed by the petitioner reflects the maximum amount of residue likely to result when the pesticide is used in the manner proposed.

The Food Additives Amendment

Also referred to as the Williams Bill (H.R. 13254), it is an Act passed on September 6, 1958, amending the Food, Drug and Cosmetic Act.

It prohibits the use of substances in food until they have been adequately tested to establish their safety. It distinguishes between food additives and food components which are not additives. Lists of substances regarded as safe and substances proposed or being regarded as safe are cleared and periodically publicized by the Food and Drug Administration.

It regulates the additives in processed food and covers any material "intentionally" or "incidentally" added to foods.

It specifies that no food additive shown to increase the incidence of cancer in humans or animals can be considered safe (the Delaney Clause).

The Nematicide, Plant Regulator, Defoliant and Desiccant Amendments of 1959

This Amendment, passed in August 1959, amended the Federal Insecticide, Fungicide and Rodenticide Act to include nematicides, plant regulators, defoliants, and desiccants under the provisions of the 1947 Act.

Pesticide Regulation Amendments, September 6, 1963

This Amendment requires warning statements on labels along with the words "Keep Out of Reach of Children" and also eliminates from the labels of all economic poisons such claims as "Safe," "Non-Poisonous," "Non-Toxic," "Non-Injurious," and "Harmless."

Public Law 88-305, May 12, 1964

This Law requires pesticide labels to bear a registration number furnished the manufacturer at the time the pesticide is approved for registration.

It eliminates the controversial "registration under protest" clause of the 1947 Federal Insecticide, Fungicide and Rodenticide Act. Under this clause it was formerly possible to register chemicals under protest even though the Secretary of Agriculture felt more information on the chemical was needed. This was long considered a major loophole in the law.

Formation of EPA — 1970

Established a new agency, the Environmental Protection Agency. Most pesticide regulatory responsibilities were transferred from USDA and FDA to EPA.

The Federal Environmental Pesticide Control Act of 1972 (FEPCA)

Legislation was signed into law on October 21, 1972. This Act substantially amended the 1947 Federal Insecticide, Fungicide, and Rodenticide Act, as amended.

It extends the requirement for registration to *all* pesticide products sold or distributed in the United States, not just those sold in interstate commerce.

It prohibits the use of any registered pesticide in a manner inconsistent with the label.

Pesticides must be classified into "general" use or "restricted" use categories. Restricted use pesticides may be used only by certified applicators.

It specifies civil or criminal penalties for violations of the Act.

Federal Pesticide Act of 1978

This Act amended the 1972 FEPCA. Several major features include:

Compensation for data requirements: Data compensation has been a major concern to both holders of the data and those who wish to use it. Reactions from the initial registrants and the potential users have been generally favorable to the compensation for data amendments. Assurance of a period of exclusive use and compensation should encourage the development of new products.

State pesticide authority: States have primary enforcement responsibilities, subject to certain important preconditions, with increased authority to approve federally registered pesticides for additional uses to meet local needs for use within that state.

Use inconsistent with labeling requirements: The 1978 law specifies that certain uses would not be considered inconsistent with labeling. These include (a) use against a target pest not specified on the label unless the label specifically states that the pesticide may be used only for pests identified on the label, (b) mixing a pesticide with fertilizer unless specifically prohibited by the labeling, (c) use of a pesticide at less than the label dosage, concentration, or frequency, (d) employing any method of application not prohibited by the label, or (e) any use that the EPA administrator determines to be consistent with the purposes of the Act. The Administrator had until May 31, 1979, to require definite label amounts of dilution for a pesticide used for agricultural or forest purposes.

Conditional registration in absence of data for complete registration: Conditional registration could be granted for: (a) a new pesticide or proposed new use which is identical or substantially similar to current registrations, for which approval would not significantly increase the risk of an unreasonable adverse effect on the environment, (b) new uses of currently registered products, subject to similar qualifications, and (c) active ingredients not contained in any currently registered products, but only to permit use of the product for a period of time sufficient to obtain the required data, and after the Administrator has determined that there would be no unreasonable risk and that the use is in the public interest.

Data requirements for minor use pesticides: Consideration will be given by the Administrator to the incentives for undertaking the development of required data for minor use pesticides. This will include appraisals of volume, pattern, and extent of use; the impact of the cost of meeting registration requirements; and the degree of exposure to humans and the environment. New rules such as waiving efficacy requirements under certain conditions, increasing state authority to register pesticides, easing labeling requirements, and allowing conditional registration should help alleviate the minor pesticide use problem.

Waiver of data requirements pertaining to efficacy: The Administrator may waive efficacy data requirements for any pesticide registration application. The 1978 Act further provides that if a pesticide is found to be efficacious by any state, a presumption is established that the Administrator shall waive data requirements pertaining to efficacy for use of the pesticide in that state.

Other features of the Federal Pesticide Act of 1978 include simplification of registration procedures, changes in classification from restricted to general use, continued state authority to certify applicators prior to completion of reregistration, permits for experimental use, and consideration of a generic approach to registration. In general, the Act was amended in an effort to streamline the pesticide regulatory process, encourage pesticide research and development, and provide greater pesticide use flexibility for growers.

Other Laws

Other laws that relate to pesticide regulation are the Federal Seed Act, 7 U.S.C. §§1551 et seq.; the Endangered Species Act, 16 U.S.C. §§1531 et seq.; the Hazardous Materials Transportation Act, 49 U.S.C. §§1801 et seq.; the Federal Water Pollution Control Act, 33 U.S.C. §§1251 et seq.; the Occupational Safety and Health Act, 29 U.S.C. §§651 et seq.; the Resource Conservation and Recovery Act of 1976, 42 U.S.C. §§6901 et seq.; and the Toxic Substances Control Act, 15 U.S.C. §§2601 et seq.

[Excerpt]

CAST

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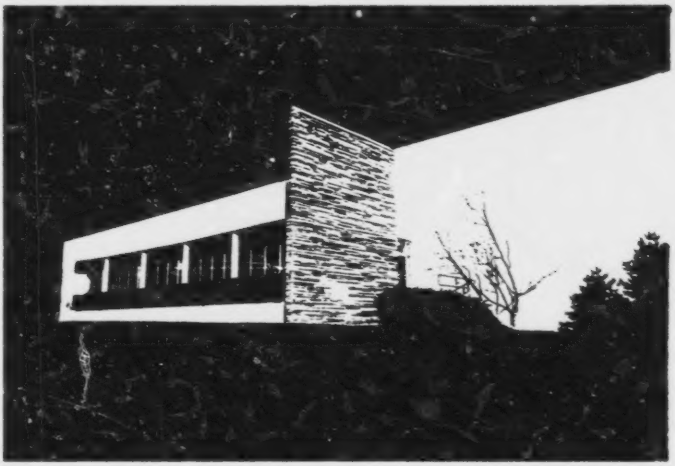
PLANT GERMPLASM PRESERVATION AND UTILIZATION IN U.S. AGRICULTURE



Council for Agricultural Science and Technology

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November 1985

developing and marketing seed products. Because this role has varied through the years and with different crops, it is convenient to review the contributions of the private seed industry by individual crops and groups of crops.

Hybrid Corn and Sorghum. When corn hybrids were first introduced, there was some uncertainty about who would produce seed. Some universities sponsored "hybrid corn schools" to educate farmers on the new development. As a result, large numbers of farmers tried seed production on a small scale. It soon became apparent, however, that hybrid seed corn production and marketing were specialized undertakings. Today, the hybrid corn industry consists of a few large companies with their own breeding programs and numerous smaller enterprises that are dependent upon the development and release of inbred lines from the public sector (Sprague, 1980). The pattern of hybrid sorghum development closely parallels that of corn; again, hybrid seed production and marketing are specialized undertakings, and virtually all improved varieties are provided by the private sector.

Self-Pollinated Crops. Since passage of the Plant Variety Protection Act in 1970, the private seed industry has played an increasing role in the breeding of self-pollinated crops, particularly soybeans. Today, while public soybean breeding programs remain strong, many seed companies are active in soybean breeding. Some seed companies are developing hybrid and open-pollinated varieties in cereals.

Cotton. The private seed industry has been a major force in cotton seed production and marketing for many years because the use of the cotton gin makes it desirable for a farmer to buy new seed rather than risk contamination from gin-run seed. The development of private breeding programs represents a natural outgrowth of industry's role.

Alfalfa. Seed production is a specialized undertaking that is separated from the primary use of the crop for forage. Today, many seed companies have alfalfa breeding programs that were developed initially as a result of effective public-private cooperation.

Future Roles and Relationships

The present cooperative relationship between public and private plant breeding institutions developed gradually and has served U.S. agriculture well. Public and private plant breeders have a common interest in increasing the efficiency of agricultural production. The question is, how may each sector contribute most productively to this common objective?

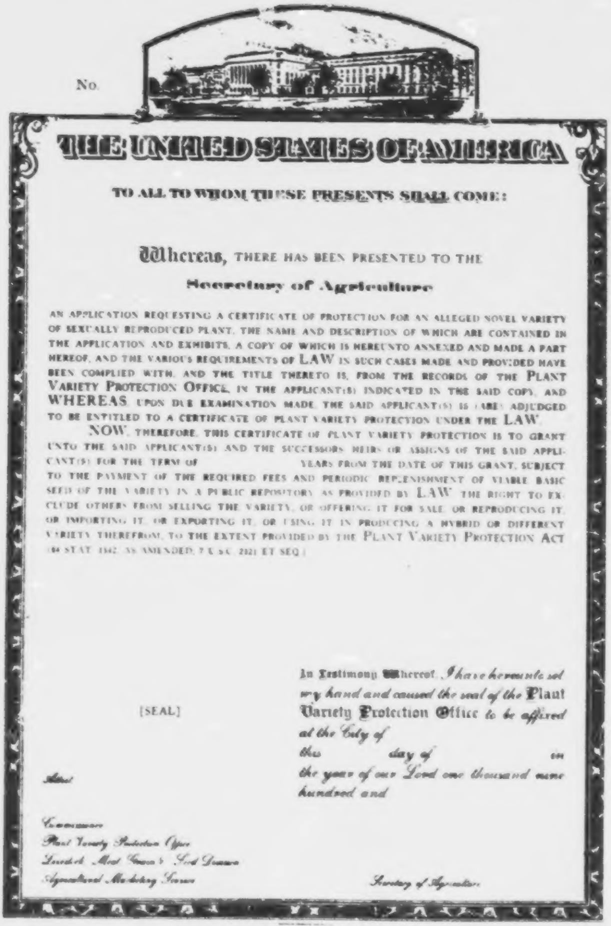
The private sector concentrates on developing superior products, primarily of species that offer promise of good return on investment. The breeding methods used by these companies generally have been developed in the public sector. Some of the large companies have the staff and resources to explore new concepts, and there may be some increase in basic research within the private sector. For the most part, however, private industry will continue to depend upon the public sector to train plant breeders, develop new germplasm, and provide the new methods necessary to increase yields, impart pest resistance, and make desirable morphological changes. At the same time, public breeding programs may continue to develop new varieties that become available to all seed producers, public and private.

The USDA and state agricultural experiment stations are in a period of reassessment and re-evaluation of their roles in plant breeding research. In 1983, the Agricultural Research Service issued a new program plan (USDA, 1983) in which its role is specified as devising new methods for modifying the germplasm of plants, beneficial organisms, and pests, and improving genetic populations of various types of crops. The role of the state agricultural experiment stations likely will be determined on a state-by-state and crop-by-crop basis. Those making decisions on agricultural experiment station policy must consider the resources available, the best interests of farmers in terms of seed costs and availability of superior varieties, and the effect on seed growers and seed companies that traditionally have produced and sold seed of varieties developed in public research programs.

Scientific plant breeding today has many new tools. In the fields of quantitative genetic theory, cell and tissue culture, and recombinant DNA technology, the roles of the public and private sectors have not yet been clarified. Research in these fields is more expensive than in traditional plant breeding, and it requires new kinds of practitioners armed with new tools and facilities. Funding for research in these areas, which comprise "genetic engineering," is developing gradually in the USDA and state agricultural experiment stations. Large seed companies are involved to some extent in the new technology. Most research in genetic engineering, however, is being done by venture capital firms—often not related to agriculture—that have been established to exploit the new technology.

Plant Variety Protection

The United States Plant Variety Protection Act (PVPA) was passed in 1970 by the U.S. Congress "To encourage the development of novel varieties of sexually reproduced plants and to make them available to the public, providing protection available to those who



No.

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

Whereas, THERE HAS BEEN PRESENTED TO THE

Secretary of Agriculture

AN APPLICATION REQUESTING A CERTIFICATE OF PROTECTION FOR AN ALLEGED NOVEL VARIETY OF SEXUALLY REPRODUCED PLANT, THE NAME AND DESCRIPTION OF WHICH ARE CONTAINED IN THE APPLICATION AND EXHIBITS, A COPY OF WHICH IS HEREUNTO ANNEXED AND MADE A PART HEREOF, AND THE VARIOUS REQUIREMENTS OF LAW IN SUCH CASES MADE AND PROVIDED HAVE BEEN COMPLIED WITH, AND THE TITLE THERETO IS, FROM THE RECORDS OF THE PLANT VARIETY PROTECTION OFFICE, IN THE APPLICANT(S) INDICATED IN THE SAID COPY, AND WHEREAS, UPON DUE EXAMINATION MADE, THE SAID APPLICANT(S) IS (ARE) ADJUDGED TO BE ENTITLED TO A CERTIFICATE OF PLANT VARIETY PROTECTION UNDER THE LAW.

NOW, THEREFORE, THIS CERTIFICATE OF PLANT VARIETY PROTECTION IS TO GRANT UNTO THE SAID APPLICANT(S) AND THE SUCCESSORS, HEIRS OR ASSIGNS OF THE SAID APPLICANT(S) FOR THE TERM OF YEARS FROM THE DATE OF THIS GRANT, SUBJECT TO THE PAYMENT OF THE REQUIRED FEES AND PERIODIC REPLENISHMENT OF VIABLE BASIC SEED OF THE VARIETY IN A PUBLIC REPOSITORY AS PROVIDED BY LAW, THE RIGHT TO EXCLUDE OTHERS FROM SELLING THE VARIETY, OR OFFERING IT FOR SALE, OR REPRODUCING IT, OR IMPORTING IT, OR EXPORTING IT, OR USING IT IN PRODUCING A HYBRID OR DIFFERENT VARIETY THEREFROM, TO THE EXTENT PROVIDED BY THE PLANT VARIETY PROTECTION ACT (84 STAT. 1542, AS AMENDED, 7 U.S.C. 2321 ET SEQ.)

In Testimony Whereof, *I have hereunto set my hand and caused the seal of the* Plant Variety Protection Office *to be affixed at the City of*
this day of in the year of our Lord one thousand nine hundred and

[SEAL]

Attest

Commissioner
Plant Variety Protection Office
Livestock, Meat, Grain & Seed Division
Agricultural Marketing Service

Secretary of Agriculture

A plant variety protection certificate. Print courtesy of Kenneth H. Evans, Commissioner, Plant Variety Protection Office, U.S. Department of Agriculture, Beltsville, Maryland.

breed, develop, or discover them, and thereby promoting progress in agriculture in the public interest." Prior to the passage of the PVPA, breeders of varieties had no legal recourse to prohibit the sale of seed of their varieties by anyone who decided to increase, advertise, and sell them.

Plant breeders' rights legislation is not unique to the United States. The PVPA was based on similar legislation passed in the United Kingdom in 1966. It was developed in the decade following the 1961 establishment of the International Convention for the Protection of New Varieties, an umbrella organization for plant breeders' rights legislation in several other countries.

Under the PVPA, the Plant Variety Protection Office of the USDA will issue a certificate of protection to the breeder of a new plant variety reproduced from seed. The certificate gives the breeder (1) the exclusive right to sell or advertise, and to license other persons to sell, seed of the registered new variety and/or the reproduction material of these plants, and (2) the right to levy and collect royalties from persons selling or using the new varieties registered under the Act.

Registration of varieties under the Act is based on international criteria of (1) novelty (distinctness), meaning the registered variety can be distinguished from all other existing varieties of the same species; (2) uniformity, meaning the registered variety does not exhibit significant variation among individuals; and (3) stability, meaning the registered variety can be reproduced truly between generations.

Participation in plant variety protection is voluntary for the breeder. Enforcement of rights is the sole responsibility of the breeder, through civil law. The government does have responsibility for enforcement of Title V of the Federal Seed Act, which allows the developer of a new variety to specify that seeds be sold by variety name only, as a class of certified seed. Upon application for protection, the breeder must submit 2500 seeds of the variety, which become the property of the Plant Variety Protection Office and are preserved in the National Seed Storage Laboratory. Although the National Seed Storage Laboratory does not distribute seed of protected varieties to breeders, seeds usually can be obtained in the open market. Breeders may use a protected variety for breeding purposes without infringing on the rights of the owner of the plant variety protection certificate.

Legal protection is extended to a variety for 18 years. If during that time the variety is needed by the public, the Secretary of Agriculture has the authority to declare it open to use and to make it available to the public. To date, the Secretary has never exercised this authority. Farmers may reproduce protected seed for their own use, provided they do not sell, offer for sale, or advertise the seed on a commercial basis. (The PVPA includes a clause known as the "farmer exemption," which allows a farmer not normally engaged in the commercial sale of seed to sell seed of a protected variety to another farmer or farmers.)

According to the Plant Variety Protection Office (unpublished correspondence), a total of 1422 certificates had been issued on 83 kinds of crops as of August 1, 1985. Of these, 60% had been issued on five crops—soybeans (335), peas (153), wheat (128), beans (123), and cotton (120).

The PVPA has not been without its critics. The issues probably were brought into their sharpest focus in 1980 in Congressional Hearings (U.S. House of Representatives, 1980; U.S. Senate, 1980). Testimony was sharply divided between those who favored plant variety protection and those who opposed it.

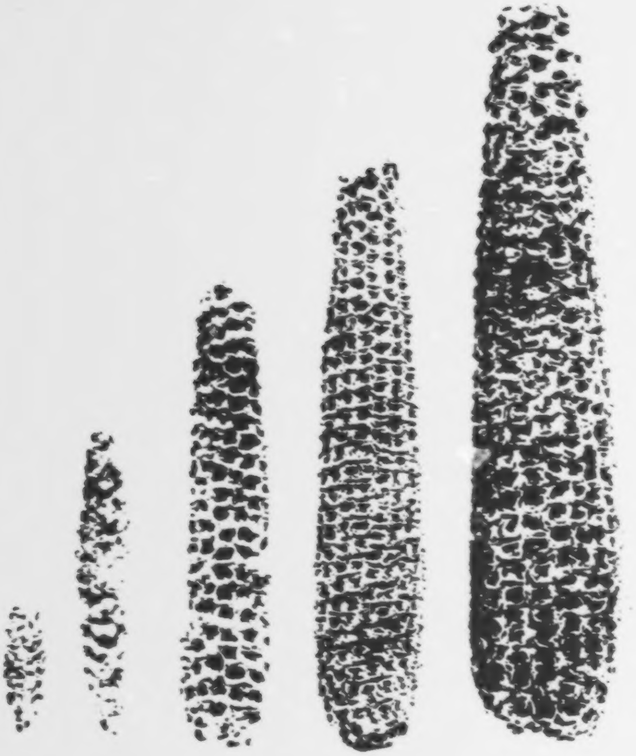
The principal issue before the House and Senate in 1980 was a proposal to remove the exemption of six vegetables from the Act. Opponents of the PVPA directed most of their criticism against the concept of plant variety protection and against the science of plant breeding, rather than limiting their criticism to the amendment to delete the exemption of the six vegetables. Many of the points raised had already been made by Mooney (1979).

Scientific concerns about plant variety protection include possible loss of germplasm resources, reduced availability of germplasm resources, reduced information flow, and increased genetic vulnerability. Economic issues include the possible impacts of the PVPA on reduction in competition in the seed industry and increases in the price of seed. These issues are difficult to analyze objectively because there is no way of knowing what would have happened if the PVPA had not been passed. Doubtless changes have occurred in these issues since passage of the PVPA in 1970; however, it is impossible to isolate the specific effects of the PVPA from the effects of all the other factors affecting agricultural seeds in the world. Accordingly, the various concerns are reviewed here from a historical perspective, with inclusion of factual evidence relating to them.

Loss of Germplasm Resources

The worldwide effort to conserve plant germplasm resources has been discussed elsewhere in this document. Loss of germplasm resources has been a continuing process through both natural selection and the plant breeding efforts of early humans, which were carried on to an impressive degree in developing recognizable varieties of wheat, barley, rice, beans, corn, and other crops. Europeans coming to North America, for example, found corn varieties adapted to nearly every part of the country. The selections made from native plants to produce these varieties were accompanied by the elimination of seed that did not have apparent worth. The enormous gene loss accompanying domesti-

28



Cobs of corn illustrating an evolutionary sequence from wild corn dated at about 5,000 B.C. on the left through cultivated types representing successively more recent times to about 1,500 A.D. on the right. Cob lengths range from 2.4 centimeters [0.9 inch] on the left to 12.5 centimeters [5.3 inches] on the right. The cobs were found preserved in caves in the Tehuacán Valley in Mexico. This evolution of corn in the hands of the Indians from a wild species to a cultivated crop that would not maintain itself in the wild was accompanied by a great loss of genes and genetic diversity. Photograph courtesy of Paul C. Mangelsdorf, Chapel Hill, North Carolina. Reprinted from Dr. Mangelsdorf's book, *Corn: Its Origin Evolution and Improvement*, by permission of the Harvard University Press.

cation of plants and animals dwarfed anything modern plant breeders have been responsible for in breeding for improved yield, quality, and pest resistance.

The loss of plant germplasm has accelerated because of the rapid growth of human populations, the urbanization of rural areas, and the increasing use of modern varieties, particularly in the Third World. The PVPA probably has had a negligible effect on the loss of world germplasm resources. The loss of germplasm, however, has been of concern to agricultural scientists and some other groups for many years. Many international, national, and private organizations have increased their efforts to collect, maintain, evaluate, catalog, and distribute genetic resources to those who need them.

Investments in Plant Breeding Research and Development

Although the intent of the PVPA was to stimulate plant breeding research and development, an examination of the research and development expenditures of plant breeding firms, the growth in the numbers of firms with plant breeding programs, and the numbers of plant breeders employed by the private sector indicates that the stimulation of plant breeding attributable to the PVPA has been very crop-specific. As inferred from the expenditures for research and development and from the numbers of applications for variety protection, the greatest quantitative impact of the PVPA has been on soybeans and wheat. (Soybeans and wheat account for one-third of all the plant variety protection certificates issued to date.)

A large number of companies started plant breeding programs in the late 1960s and 1970s; however, these newer companies represent a relatively small proportion of the total research and development expenditures, and they share in a relatively small percentage of the total plant variety protection certificates issued since the PVPA was enacted. Most of the total research and development expenditures have been made, and most of the plant variety protection certificates are held, by seed companies with large plant breeding programs established prior to enactment of the PVPA.

Research and development investments by seed companies increased most rapidly during the period from 1967 to 1970, possibly in anticipation of passage of the PVPA. During the 1970s, increases in research and development expenditures approximately kept pace with increases in seed sales. There is little evidence to suggest that total research and development activity has increased faster than it would have without the PVPA.

The PVPA may have had a modest impact on publicly supported plant breeding research. There may have been a slight shift in state agricultural experiment station plant breeding and genetic research monies toward basic research, but the evidence is not conclusive. Many state agricultural experiment stations have protected a few new varieties, but participation of the public sector in plant variety protection has been slight relative to that of the private sector. Some plant breeders in the public sector feel that protection of publicly developed varieties is in conflict with the mission of a publicly funded research institution. The majority of publicly developed varieties that have been protected have no restrictions on who may produce them, however, so that all companies have access to them.

Availability of Germplasm Resources and Information Flow

The PVPA results in increased commercial value for scientific information and breeding materials, and for this reason it might be expected to decrease germplasm availability and information exchange. Prior to the passage of the PVPA, it was felt by many (including many seedsmen) that such legislation would result in a reduction in the flow of scientific information and exchange of germplasm. The length of time required to develop a new plant variety can vary from 7 to 12 (and up to 20) years. Useful scientific information and genetic materials may be developed at any stage in this process. Exchange of information may occur during the developmental process as well as after a new variety is released.

Without some type of legal protection, a new privately developed variety will provide its developer some monopoly advantages for only 1 or 2 years. If a new variety is promising, other companies will quickly produce seed and add the variety to their list of offerings. When the developing company has lost its exclusive marketing advantage, there is less incentive to conceal the genetic make-up of the new variety and the breeding techniques used to develop it. In addition, without patent-like protection, scientific findings made during the development process have less potential monetary value and hence are more likely to be shared.

The amount of scientific information and plant breeding materials sent from universities to other universities and to private companies increased during the 1970s, but the flow from companies to universities decreased, perhaps in part as a result of the PVPA. Given the increased value to private companies of scientific developments as a result of the PVPA, private plant breeders would be expected to be more active in searching out and obtaining information and germplasm from public plant breeders. The mechanisms for exchanging scientific materials may also have improved during the 1970s. The effect, however, would be expected to vary widely across species, depending upon the dominance of public or private breeding efforts.

Genetic Vulnerability

Genetic vulnerability (see also page 4) is an important issue that transcends plant variety protection. According to the National Plant Genetic Resources Board, the best defense against genetic vulnerability is to maintain many active plant breeding programs with a reserve of material in all phases of breeding from unimproved germplasm to nearly finished varieties. If plant variety protection results in more plant breeding programs and more plant breeders working on individual crops, it should result in greater insurance against genetic vulnerability.

Competition in the Seed Industry

Although theoretically there are grounds for expecting that the PVPA may lead to increasing domination of the seed market by a few companies, there is little evidence to suggest that current market shares of privately protected varieties or of leading companies seriously hamper competitive market forces in the seed trade. The numbers of acres planted with seed of protected varieties are a relatively small part of the total for most crops. Unprotected varieties still dominate many crops and are available for seed companies to produce and market. Thus, while plant variety protection confers statutory monopolies on owners of protected varieties, this currently results in little market power because of the large numbers of unprotected and public varieties in the market from which buyers can choose.

For some crops, a few companies own a high percentage of the plant variety protection certificates. If the crop is one with a large number of protected varieties (e.g., soybeans), the extent to which certificates are concentrated in the hands of a few companies may provide some indication of what might happen in the future in the way of control of the seed market for these crops. This is particularly true in those crops with little publicly supported breeding research.

There is little doubt that the PVPA does provide a mechanism for increasing market power. This is part of the intent of any patent system. If, in the future, most of the seed sold for some crops is of privately protected varieties, some increase in market control probably will occur. Competitive market forces then may be hampered to some extent. When and to what extent this may happen is uncertain.

Entry barriers to plant breeding in the seed industry are now relatively low because the seed market for most crops is still dominated by publicly developed and unprotected varieties. However, if agricultural experiment stations and other public plant breeding institutions reduce their output of finished varieties in the future, and many of the anticipated developments in genetic engineering are realized, the entire structure of the seed industry may change, and barriers to entry may become prohibitively high.

The PVPA may have contributed to the large number of mergers and takeovers involving seed companies in the 1970s. But the PVPA appears to be less important than the desire to acquire companies and merger partners for diversification. A number of other factors have made seed companies attractive acquisition targets — particularly the development and growth of biotechnology.

Merger and takeover activities have ranged from simple mergers of small seed companies striving to capture some economies of scale, to the takeover of several of the largest seed companies by large corporations, some of which are transnational conglomerates. Large conglomerates are now an important force in the seed industry. By 1982, nearly 50% of the plant variety protection certificates issued were held by 14 conglomerates. The impact of conglomerates on the seed industry, however, has not been documented sufficiently to permit a defensible conclusion.

Seed Prices

A number of questions have been raised about the impact of the PVPA on seed prices. An increase in seed prices should not necessarily be regarded as an unexpected or undesirable result of the PVPA. Indeed, one of the purposes of the PVPA is to permit seed companies to recoup fair returns on their investments in research and development of new plant varieties. It may also be presumed, since the intent of the PVPA is to encourage new and novel varieties of better quality, that farmers would be willing to pay more for "better" varieties. The issue, then, is not merely a change in prices, but whether or not plant variety protection has triggered structural changes that create or are likely to create sustained unjustifiably high prices.

Although seed prices have increased sharply since 1970, it would be misleading to attribute all of the price increase to enactment of the PVPA. The PVPA is expected to affect primarily the prices of privately protected varieties of sexually reproduced crops. These varieties account for a very small proportion of the seed sold. For example, in 1980, privately protected varieties accounted for 3% or less of the acreage planted to wheat, barley, and rice, and about 10% of the soybean acreage. Even large increases in the prices of privately protected varieties would have little influence on the index of prices paid for all seeds.

In most crops, there are two important checks on the prices of privately protected varieties. First, bin-run or farmer-saved seed is a viable alternative for many crops (e.g., cotton, soybeans, and most cereals). Although certified seed is generally somewhat higher in quality, farmers are likely to pay only a limited premium. For some other seeds, such as alfalfa, clover, and many vegetables, it is not feasible for most farmers to save their own seed. Pricing discretion is much greater on privately protected varieties of these seeds.

The other check on the prices of many seeds is the availability of publicly developed varieties. The future effects of the PVPA on seed prices are likely to be of greatest concern in those crops where neither of the above constraints is present.

If farmers are fully informed and able to evaluate accurately the value of privately protected varieties relative to that of unprotected and publicly developed varieties, the premium they are willing to pay for a protected variety will not exceed the increased value it represents. Under these conditions, the cost of seed per unit of farm output would decline or hold constant as a result of protected varieties. Limited evidence from industry sources indicates that seed price increases have not fully captured the value to farmers of genetic improvements. To the extent that this is generally true, seed cost per unit of farm production has declined. Some of the monetary benefits of genetic improvements have been realized by farmers and society.

It is difficult to evaluate precisely the influence of the PVPA on the seed trade and society in general because so many other factors are involved. It can be safely concluded that the PVPA has had a positive impact on private plant breeding efforts in several crops, but that it has not triggered massive investments in private plant breeding. There is little evidence that substantial public costs have resulted from the PVPA. The influence of the PVPA on increases in seed prices, market concentration and advertising, declines in information exchange and public plant breeding, genetic vulnerability, and loss of plant germplasm resources has been either nil or modest. Thus it appears that the PVPA has resulted in modest private and public benefits at modest public and private costs. If a reasonable balance is maintained between the public and private sectors in the breeding of most crops, the present balance of benefits and costs should continue.

Implications of the New Biological Technologies

The emerging biotechnologies may have profound implications for agriculture. For example, it has been suggested that genetic engineering and cell fusion provide scientists the potential to engineer plants that fix their own nitrogen, have resistance to a wide range of pathogens, have improved tolerance to drought and higher levels of salt, and have a perennial growth habit.

Some of these suggestions may be unrealistic, or, at best, very long-term endeavors. Nonetheless, it seems reasonable to expect that the new techniques will enable plant scientists to develop novel strains and species of plant life that may increase the demand for exotic germplasm as the search widens for new and more desirable genetic traits.

Genetic engineering has the potential for decreasing the genetic vulnerability of crop species. Conversely, it could reduce the genetic diversity of crop species if a new variety produced by some genetic engineering technique should prove so superior that it would result in the demise of a number of competing varieties.

The potential of the emerging biotechnologies and associated techniques is not a cause for complacency with regard to preservation and utilization of plant germplasm. Rather, the advances to be expected will place new demands on our national plant germplasm system.

Future Needs

Methods of Evaluating and Utilizing Germplasm Collections

Developing evaluation methods that will facilitate the use of current and future germplasm collections is a major challenge. Such methods must answer the needs of the plant breeder.

Plant breeders are interested primarily in improved performance, with increased yield generally a major component. Development of improved selection criteria has been a continuing process, but visual factors that are closely associated with yield have yet to be identified.

The breeder would like to know how each new germplasm accession compares with one or two improved varieties of known performance. In self-pollinated crops, a direct visual comparison of each new accession with standard varieties as controls would be most valuable. Planting a control beside or close to each new germplasm source on uniform soil with good culture would enable the breeder to assess the comparative times required to reach maturity and the presence of such characters as relative plant height, resistance to lodging, and resistance to any pests that may be present.

In cross-pollinated crops, particularly those using cytoplasmic male sterility to produce commercial F_1 hybrids, the breeder needs additional information on a new accession. Will it maintain cytoplasmic male sterility or restore fertility? How variable is it? How great is the depression of yield that occurs upon inbreeding? Does it harbor recessive genes for short stature, disease resistance, or other significant characteristics that cannot be seen until it is self pollinated? What kind of performance will an accession give when it is crossed with the best cytoplasmic male sterile line in general use?

To answer the foregoing questions, seed derived from self pollination of the new accession must be crossed with the cytoplasmic male sterile line. Appropriate comparative plantings then must be made and evaluated.

Many genes providing resistance of crops to diseases and insects are recessive. In cross-pollinated crops, this means the desired trait cannot be seen until the germplasm is carried to the S_1[3] generation. Storing some germplasm from cross pollinated crops in the S_1 condition would greatly facilitate rapid screening by breeders.

Mixing the S_1 seed of a number of accessions reduces the amount of material to be handled and facilitates the search for desired genotypes and genes. This procedure was used by Burton (1978), for example, to produce a composite sample of pearl millet germplasm that consisted of a mixture of seed resulting from the self pollination of 275 pearl millets from Africa and India. The mixture, which contained a great variety of dominant and recessive characters, proved valuable to one breeder who was able to select 16 different types of plants (genotypes) suitable for his use.

Personnel and Facilities

The main components of the National Plant Germplasm System and the special germplasm collections are understaffed. Scientists and support personnel trained for preserving plant germplasm resources are in short supply.

The most effective utilization of plant germplasm in crop improvement involves the participation of specialists from many scientific disciplines—plant breeders, plant geneticists, botanists, entomologists, nematologists, microbiologists, agronomists, and horticulturists. All of these scientists must rely on the best taxonomic information available within their respective areas of expertise. Taxonomic research and service thus represent an additional area of major importance.

If adequately staffed, each Plant Introduction Station would have a research leader/coordinator, agronomist, horticulturist, plant pathologist, entomologist, and geneticist, together with appropriate support personnel to handle the required documentation, laboratory, and field work. The National Seed Storage Laboratory would have additional scientific, technical, and clerical support. Some curators of special germplasm collections, especially the larger collections, would have additional staff at all levels. Improved staffing should increase efficiency in use of the collections through improved evaluation and documentation of the accessions and a reduction in unwarranted duplication.

Facility priorities for several components of the Germplasm System were discussed by Murphy (1981). The high-priority special facilities he mentioned include an expansion of the National Seed Storage Laboratory at Fort Collins, Colorado, new facilities for the Small Grains Collection at Beltsville, Maryland, development of facilities for the rest of the planned clonal repositories, and a germplasm center at Beltsville, Maryland. Not included in his review were the facility priorities of curators of many of the special germplasm collections. These include improved storage conditions, additional office, greenhouse, and/or laboratory space, emergency greenhouse heating and electrical systems, new or replacement farm equipment, and harvesting and cleaning equipment.

Murphy (1981) and Stanwood and Bass (1981) reviewed the situation at the National Seed Storage Laboratory. Storage space will be filled by 1988 at the present rate of acquisition. Space for offices, seed cataloging, seed packaging for storage and germination testing, and research laboratories is overcrowded. Little space is available that can be converted for storage of seeds at very low temperatures.

The Small Grains Collection is presently housed in a very old building with limited work space. Murphy (1981) recommended a new facility for this collection.

The National Plant Germplasm Committee has developed plans for a system of clonal repositories for plant germplasm that cannot be preserved as seeds. Several clonal repositories are planned because not all vegetatively propagated crops can be maintained economically at a single location. Of the eight (originally 12) clonal repositories planned, five are presently in operation (Jones and Gillette, 1982; Murphy, 1981; Science and Education Administration, 1977; unpublished information).

Present facilities for plant germplasm activities at Beltsville are scattered and inadequate. According to Murphy (1981), construction of a "Germplasm Center" to house what now are called the U.S. Plant Introduction Quarantine Station, the Plant Introduction Office, the Germplasm Resources Information Network Database Management Unit, and the Plant Exploration and Taxonomy Laboratory could provide adequate work space for each activity.

The Science and Education Administration (1977) identified the development of facilities in a tropical location as a high priority need. Such facilities would be used to multiply seed of plants that must be grown under tropical conditions, and to maintain some clonal material, such as tropical grasses and peanut germplasm, that must be maintained in a frost-free area as living plants because of poor seed production. A significant amount of germplasm now present in various

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[3] The term S_1 refers to the seed or the first generation of plants grown from the seed resulting from self-pollinating a plant or a group of plants.

DIVISION OF AGROCHEMICALS
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November 20, 1985

The Honorable Charles McC. Mathias
Patent, Copyright & Trademarks Subcommittee
United States Senate
SD-137 Dirksen Bldg.
Washington, DC 20510

Dear Senator Mathias:

The Agrochemicals Division of the American Chemical Society wishes to express its support for Senate Bill 1093, the Agricultural Patent Reform Act of 1985. The Officers and the Executive Committee of the Division were unanimous in their vote directing me to inform you of our attitude in this matter.

The Agrochemicals Division is constituted of professional chemists in the field of crop protection chemicals and related agrochemicals. Our members come from universities, government, and industry. We are all very much aware of the tremendous amount of research that has to be conducted between the date that a new agricultural chemical is discovered, and the date on which it is registered for first sale in the United States. This research is important, expensive, and time consuming. It is in the best interests of all concerned, especially the citizens of the United States, that it be done thoroughly and well. It is only appropriate, therefore, that the inventors be permitted to enjoy a normal length of patent protection for their invention, beginning at the time that registration occurs. Although the expense of 7-9 years of research to establish environmental and public health safety must still be paid by the inventors and their backers, the elapsed time required to conduct this vital research must not continue to be subtracted from the useful life of the patent. Unless such a provision is made to protect the inventors and producers of new agriculturally useful chemicals, the combination of increasing time for research required before registration and corresponding decrease in useful patent life will seriously impede the development and introduction of more effective and safer chemicals for agriculture.

Respectfully yours,

John Harvey, Jr.

John Harvey, Jr.

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

DEC 9 1985

Honorable Charles McC. Mathias, Jr.
United States Senate
Washington, DC 20510

Dear Senator Mathias:

Reference is made to your November 12 letter regarding patents on agricultural technology development.

The ability to patent agricultural chemicals and products of biotechnology is essential for the advancement of American agriculture. Patent protection stimulates people and organizations to invest in research and development and provides competitive incentives to find new products and processes. Rather than stifling innovation, patents encourage competition to constantly find better products and improvements to service U.S. agricultural production and technology.

In the absence of patent protection, it is doubtful that any organization, large or small, would find justification in investing significant resources and dollars required to develop and market a new product or process. Especially noteworthy are the lengthy and costly procedures involved in complying with registration requirements of Federal agencies such as the U.S. Environmental Protection Agency and the Food and Drug Administration.

Recent federal licensing reforms have liberalized exclusive licensing opportunities which provide further incentives for private sector adoption of public patented technologies. Currently, as a result of these policies, 29 exclusive licenses have been granted to industry, by the U.S. Department of Agriculture, in order to expedite commercialization of the research. These licenses will result in industry investing $30 million in capital to bring the technology to the market place.

Sincerely,

C. MICHAEL HOBACK
Confidential Assistant
to the Assistant Secretary
for Science and Education

NEWSPAPER ARTICLES

[From the Delmarva Farmer, Aug. 6, 1985]

MOMENTUM FAVORING AG CHEMICAL FIRMS' PREDICAMENT

THE AGRICULTURAL PATENT REFORM ACT

Legislation to restore to agricultural chemicals at least a portion of the patent "life" of a new product, which manufacturers now lose in the time devoted to research and development, is gaining support in the agricultural industry.

All patents carry a term of 17 years. That is, a patented product is protected against duplication for 17 years. However, ag chemicals, guarded by strict federal regulation, typically take five to seven years to get to market and those years, under present legislation, are subtracted from the 17-year patent term.

The ag chemical industry argues, from a variety of standpoints, that that is a harsh and inequitable penalty.

And Maryland's Sen. McC. Mathias has introduced legislation to correct it.

The so-called Agricultural Patent Reform Act, of which Delaware's Sen. Joe Biden is among the 15 or so cosponsors, was the subject of a recent conference in Easton, Md.

Attending were Luther W. Shaw, vice president for public affairs of the National Ag Chemicals Association; David Modi, counsel for E.I. DuPont's Washington, D.C. office; Ed Covell, representing the Maryland Ag Commission; Wade Dudrow, president of the Talbot County Farm Bureau and representing the Maryland Farm Bureau; and Allen Davis, a Kent County farmer and president of the Maryland Grain Producers Association.

The Mathias bill would restore, up to a maximum of five years, the time lost on a ag chemical patent for its required formulation, research and development and in obtaining EPA approval.

The position of the National Ag Chemicals Association (NACA) on the patent term restoration is basically this:

NACA seeks patent term restoration as a matter of equity. It would restore part of the patent term that is lost to those products that must meet federal regulatory requirements before they can be marketed.

To put it simply, unregulated patented products are free to receive the full 17 years of patent protection set by Congress. NACA members companies manufacture or formulate virtually all of the crop protection chemicals produced in the U.S. All of these agrichemicals are subject to federal regulatory requirements which typically prevent them from receiving the full 17 years of patent protection in the marketplace because these products cannot be sold commercially until federal approval is obtained.

Recent studies show that the average time for completion of the regulatory review process for an agrichemical is five to seven years. Thus, agrichemicals are realizing far less patent protection than Congress originally intended.

Significantly, the shortened patent life caused by regulatory review acts as a disincentive to innovation, according to NACA. If a company has a unique product, it has only the remaining time of the patent life to recoup the invested capital and regain all other costs and expenditures, and generate sufficient return to continue in business.

With the research and development costs of agricultural chemicals now in the $25 to $35 million range per product, the matter of equity stands out even more starkly since the agricultural chemical producer does not enjoy the fruits of the full patent term that the unregulated patented producer in other businesses does, NACA claims.

A NACA survey of member companies found that nearly all considered a favorable patent position a critical factor in deciding whether to invest in new product development. The survey also indicated that the availability of patent protection is a highly important element in long-range research planning and funding. Respondents noted that the uncertainty, cost and delay caused by the governmental regulatory process have caused a reduction in research efforts.

If this deterioration continues, NACA says, the impact on the U.S. will be negative in economic terms and also in our nation's ability to meet domestic and international food requirements.

This is Sen. Mathias' third try at patent reform. An earlier version, in 1982, failed by five votes, and the 1983 Senate bill was introduced late in the session and ran out of time.

Mathias, addressing the Senate at the introduction of the current legislation (Senate Bill 1093) had these comments:

"In the earlier versions of this bill, the coverage included both pharmaceutical drugs and agricultural chemicals, such as pesticides and fertilizers. These agrichemicals also lose an average of five to seven years of their patents because of premarket regulatory review requirements imposed by the EPA.

"Last year, we separated the agrichemical portion of the bill from the pharmaceutical bill because the latter became coupled with amendments on generic drugs, and the agrichemical provisions no longer fit neatly into the package. A separate bill was introduced late in the session last year in the House and Senate, but we ran out of time.

"A solid legislative record has been built for agrichemical patent restoration in hearings over the past two Congresses, and I would hope to hold an early hearing this year to bring the record up to date.

"Fairness is the primary goal of this bill. The inventor of an agrichemical product should get the same treatment under our patent laws as any other invention. But it is important to remember the reason for the patent laws in the first place: the principle that exclusive rights for limited times is the best way to promote scientific progress in the useful arts, the principle embodied in Article I, Section 8 of our Constitution. Giving fuller patent life to inventions in the agricultural field will stimulate greater research and innovation."

Among those backing patent term restoration for ag chemicals is Maryland Secretary of Agriculture Wayne Cawley, Jr.

In a recent letter to Mathias, Cawley remarked:

"It is my understanding that this will help agricultural chemical producers regain their investment capital from product research. This can only be beneficial to agriculture as it will encourage more research and ensure the development of improved chemicals which will be more efficient and inevitably have less impact on the environment."

Most farm and ag-related trade associations in the nation backed patent reform legislation in earlier congressional attempts at it, including the American Farm Bureau Federation, the National Farmers Organization, the National Farmers Union, the National Corn Growers Association and the American Soybeans Association.

Most are expected to do so again, according to NACA's Shaw.

Mathias is chairman of the Senate's Subcommittee on Patents and is expected to call hearings on the bill this fall. "It is our hope," said DuPont's Modi, "that the bill can be brought to the full Senate for consideration before the end of the year."

Mathias' 1984 bill reportedly ran into some opposition from the manufacturers of generic ag chemicals, those chemicals that have run their patent life and are, therefore, eligible for manufacture by other than their originators.

However, Modi said, a compromise appears to have been reached—the maximum five-year restoration clause, for example—which will allow the generic manufacturers to support the current legislation.

"They realized," explained Modi, "that if fewer and fewer ag chemicals reach the market from their developers, there will be fewer and fewer capable ultimately of generic production."

Davis and Dudrow said they were unable, at that point, to express a viewpoint on the legislation on behalf of their organizations—the Maryland Farm Bureau and the Maryland Grain Producers—since their directors, to their knowledge, had not taken a formal position on it.

However, as farmers, each commented that patent reform was needed to encourage the continued development of newer and safer chemicals and to guarantee a continued flow of products into the generic marketplace.

[From the Delmarva Farmer, Aug. 13, 1985]

Comment

THE "AGRICULTURAL PATENT REFORM ACT"

Maryland's Senator McC. Mathias has introduced a bill which bears the title "Agricultural Patent Reform Act."

The bottom lines of the legislation are these: all patents carry a patent protection "life" of 17 years.

The term of the patent begins when application for it is made and filed. Under current law, the agricultural chemical industry is penalized, often for more than half of the 17 years, because of the time it takes to develop—and then win EPA approval—of a new pesticide, is deducted from the patent term.

The Mathias bill, among whose 15 or so co-sponsors are Senators Joe Biden of Delaware and Arlen Specter of Pennsylvania, would restore up to a maximum of five years of those subtracted for research, development and EPA labelling approval.

From our vantage point, the bill would correct any number of flaws evident, or inherent, in current legislation. Our principal concern, however, is equity—or rather the lack of it—under which ag chemical producers and marketers must now produce and market.

The shortened patent life caused by federal regulatory review (and there's no argument here about the need for that review) acts as a disincentive to innovation. If a company has a unique and innovative product, it has only the time remaining of the patent life to recoup its invested capital and regain all other costs and expenditures and generate sufficient return to continue in business.

With the research and development cost of ag chemicals now in the $25 to $35 million range per product, the matter of equity stands out starkly. The ag chemical producer does not enjoy the fruits of full patent term that the unregulated patented producer in another business does.

What's good for the goose, it seems to us, is good for the gander. If a person builds a better mousetrap and gets a 17-year patent term, so should the ag chemical industry.

We assume that Senator Mathias will soon schedule public hearings on the bill before the Patent Subcommittee of the Senate, of which he is chairman. And it is our hope that the measure can be moved quickly to the Senate floor for action—and approval—before the end of the year.

With the kind of bucks that are being spent to produce safer and more effective crop protection chemicals, time's a wastin'.

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